

# Protein network study of human AF4 reveals its central role in RNA Pol II-mediated transcription and in phosphorylation-dependent regulatory mechanisms

Gabriella ESPOSITO\*<sup>†</sup>, Armando CEVENINI\*<sup>†</sup>, Alessandro CUOMO\*, Francesca DE FALCO<sup>‡</sup>, Dario SABBATINO<sup>†</sup>, Fabrizio PANE\*<sup>†</sup>, Margherita RUOPPOLO\*<sup>†</sup> and Francesco SALVATORE\*<sup>‡</sup><sup>1</sup>

\*CEINGE-Biotecnologie Avanzate, s.c.a.r.l., Via G. Salvatore 486, 80145 Naples, Italy, <sup>†</sup>Dipartimento di Biochimica e Biotecnologie Mediche, Università di Napoli "Federico II", Via S. Pansini 5, 80131 Naples, Italy, and <sup>‡</sup>IRCCS-Fondazione SDN, Via E. Gianturco 113, 80143 Naples, Italy

AF4 belongs to a family of proteins implicated in childhood lymphoblastic leukaemia, FRAXE (Fragile X E site) mental retardation and ataxia. AF4 is a transcriptional activator that is involved in transcriptional elongation. Although AF4 has been implicated in MLL (mixed-lineage leukaemia)-related leukaemogenesis, AF4-dependent physiological mechanisms have not been clearly defined. Proteins that interact with AF4 may also play important roles in mediating oncogenesis, and are potential targets for novel therapies. Using a functional proteomic approach involving tandem MS and bioinformatics, we identified 51 AF4-interacting proteins of various Gene Ontology categories. Approximately 60% participate in transcription regulatory mechanisms, including the Mediator complex in eukaryotic cells. In the present paper we report one of the first extensive proteomic studies aimed at elucidating AF4 protein cross-talk. Moreover, we

found that the AF4 residues Thr<sup>220</sup> and Ser<sup>212</sup> are phosphorylated, which suggests that AF4 function depends on phosphorylation mechanisms. We also mapped the AF4-interaction site with CDK9 (cyclin-dependent kinase 9), which is a direct interactor crucial for the function and regulation of the protein. The findings of the present study significantly expand the number of putative members of the multiprotein complex formed by AF4, which is instrumental in promoting the transcription/elongation of specific genes in human cells.

**Key words:** acute lymphoblastic leukaemia, AF4–ENL–P–TEFb complex (AEP complex), AF4 interactome, Mediator complex, mixed-lineage leukaemia chimaera (MLL chimaera), protein–protein interaction, RNA polymerase II-mediated transcription elongation.

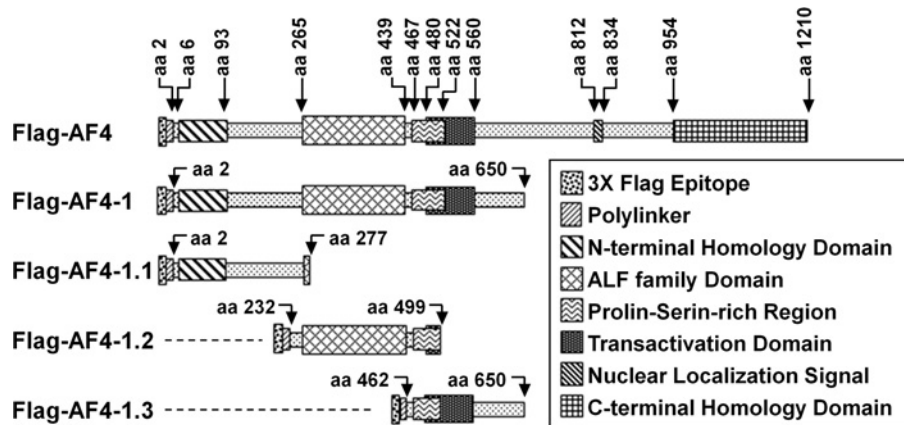
## INTRODUCTION

*AF4* is the prevalent (37%) MLL (mixed-lineage leukaemia) fusion gene associated with spontaneous acute lymphoblastic leukaemia [1,2]. The *AF4* gene transcript is ubiquitously expressed in all types of haemopoietic cells and in other human tissues, including brain [2,3]. The AF4 protein is a member of the ALF [AF4/LAF4 (lymphoid nuclear protein related to AF4)/FMR2 (Fragile X E mental retardation syndrome)] family of nuclear proteins, which include AF4, AF5q31, LAF4 and FMR2 [4–8]. *AF4*, *AF5q31* and *LAF4* form fusion genes with *MLL* in leukaemia [9]. There are three regions that are conserved in ALF family members: the N-terminal homology domain, the ALF domain, which contains a proline/serine-rich region, and the C-terminal homology domain (Figure 1) [9]. Furthermore, all of the ALF family members, except FMR2, have a transactivation domain [9]. The ALF domain seems to promote ALF protein degradation through the proteasome pathway by mediating their interaction with SIAH (seven in absentia homologue) ubiquitin ligases [10,11]. A murine AF4-knockout model demonstrated that AF4 is important for normal lymphocyte development and cell growth [12]. Furthermore, *Af4* was identified as the disease gene in the robotic mouse, a dominant *N*-ethyl-*N*-nitrosourea mutant that, in addition to defects in early T-cell maturation,

develops ataxia because of Purkinje cell degeneration in the cerebellum [13]. This finding suggested that AF4 plays a hitherto unknown role in a function of Purkinje cells that is essential for the control of balance and motor co-ordination [14]. Moreover, AF4, also through the interaction with the P-TEFb (positive transcription elongation factor b) [15], ENL and/or AF9 [5], was found to have transcriptional regulatory properties that entail elongation and chromatin remodelling involving Pol II (RNA polymerase II) [15]. Of note, the ENL family proteins ENL and AF4 associate with DOT1L, the histone methyltransferase that modifies H3K79 and marks actively transcribed genes [15]. A recent study demonstrated that AF4 belongs to a higher-order multiprotein complex, which is constituted by at least P-TEFb, ENL and AF5q31 (the 'AEP complex'). This multiprotein complex is recruited by wild-type MLL only on some of its target promoters [i.e. *HOXA9* (homeobox A9) and *MEIS1* (myeloid ecotropic viral integration site 1 homologue)] [16] by context-dependent mechanisms that are still unknown. In contrast, chimaeric oncoproteins originating from the fusion of MLL with AEP components (MLL–AF4, MLL–AF5q31 and MLL–ENL) constitutively form hybrid complexes to cause sustained expression of MLL-target genes that leads to leukaemic transformation of haemopoietic cells [16].

Abbreviations used: aa, amino acids; AEP complex, AF4–ENL–P–TEFb complex; ALF, AF4/LAF4 (Lymphoid nuclear protein related to AF4)/FMR2 (Fragile X E mental retardation syndrome); bp, base pairs; CDK9, cyclin-dependent kinase 9; CTD, C-terminal domain; ECL, enhanced chemiluminescence; ELL, eleven-nineteen lysine-rich leukaemia; EAF1, ELL-associated factor 1; FBS, fetal bovine serum; FMR2, Fragile X E mental retardation syndrome; HEK, human embryonic kidney; HOXA9, homeobox A9; HPRD, Human Protein Reference Database; LAF4, lymphoid nuclear protein related to AF4; LC-ESI, liquid chromatography-electrospray ionization; MCM, minichromosome maintenance; MED, Mediator complex subunit; MLL, mixed-lineage leukaemia; MS/MS, tandem MS; PICM, protease inhibitor cocktail for mammalian tissues; Pol II, RNA polymerase II; P-TEFb, positive transcription elongation factor b; SEC, super elongation complex; SIAH, seven in absentia homologue; WCE, whole cell extract.

<sup>1</sup> To whom correspondence should be addressed (email salvator@unina.it).



**Figure 1** Schematic representation of the flagged AF4 constructs used in the present study

The various known protein domains are shown.

In the present study, we used functional proteomics procedures to look for proteins that interact with human AF4 in an attempt to gain further insights into its function and the regulatory mechanism in which it is involved in physiological, as well as in pathological, transcriptional pathways.

## EXPERIMENTAL

### Plasmids

The full-length *AF4* cDNA (GenBank<sup>®</sup> accession number NM\_005935) and partial *AF4* cDNAs, designated AF4-1 [bp (base pairs) 4–1950; aa (amino acids) 2–650], AF4-1.1 (bp 4–833; aa 2–277), AF4-1.2 (bp 696–1497; aa 232–499) and AF4-1.3 (bp 1384–1950; aa 462–650), were cloned into the N-terminal p3X-FLAG 7.1 vector (Sigma–Aldrich), to obtain recombinant proteins tagged with a FLAG epitope at the N-terminus (Figure 1). Primer sequences and cycling conditions are available upon request from the corresponding author.

### Antibodies

The antibodies used were: mouse monoclonal anti-FLAG M2 and anti- $\alpha$ -tubulin (Sigma–Aldrich); rabbit polyclonal anti-AF4 for immunoprecipitation and anti-AF4 for Western blotting (Bethyl Laboratories); rabbit polyclonal anti-CDK9 (cyclin-dependent kinase 9), anti-ELL (eleven-nineteen lysine-rich leukaemia), anti-YWHAQ, anti-YWHAE, anti-MED1 (MED is Mediator complex subunit) (Santa Cruz Biotechnology); goat polyclonal anti-MED7, anti-CRSP3 (also known as MED23), anti-SIAH-1, anti-MED27, anti-MED24, anti-MED17, anti-MED6 and anti-MED26 (Santa Cruz Biotechnology); anti-mouse and anti-rabbit secondary antibodies (GE Healthcare); and anti-goat secondary antibody (Santa Cruz Biotechnology).

### Cell culture and transfection

HEK (human embryonic kidney)-293 cells (A.T.C.C. number CRL-1573) were grown in DMEM (Dulbecco's modified Eagle's medium; Lonza), supplemented with 10% FBS (fetal bovine serum; Lonza) and 10 ml/l penicillin/streptomycin (Sigma–Aldrich). Cells were seeded for 24 h before transfection at approximately  $6 \times 10^4/\text{cm}^2$  confluency and transfected for 48 h using the calcium phosphate method. 697 cells (human pre-B lineage leukaemia) [DSMZ (Deutsche Sammlung von

Mikroorganismen und Zellkulturen) number ACC 42] were cultured in RPMI 1640 medium (Lonza) supplemented with 20% FBS (Lonza), 2 mM L-glutamine (Sigma–Aldrich) and 10 ml/l penicillin/streptomycin (Sigma–Aldrich).

### Cell lysis, protein extraction and immunoprecipitation

HEK-293 cells were transfected with either a recombinant or empty vector (mock control) and lysed in immunoprecipitation buffer A [10% glycerol, 50 mM Tris/HCl (pH 8), 150 mM NaCl, 0.1% Nonidet P40, 0.5 M EDTA and 10  $\mu\text{l}/\text{ml}$  PICM (protease inhibitor cocktail for mammalian tissues; Sigma–Aldrich)]. 697 cells were lysed in immunoprecipitation buffer B [50 mM Tris/HCl (pH 8), 150 mM NaCl, 10 mM KCl, 1.5 mM  $\text{MgCl}_2$ , 10 mM sodium fluoride, 1.5 mM  $\text{MgCl}_2$ , 1 mM sodium orthovanadate, 0.2 mM EDTA, 0.5% Nonidet P40 and 10  $\mu\text{l}/\text{ml}$  PICM].

For the FLAG immunoprecipitation assays, the lysate was incubated for 1 h at 4°C with anti-FLAG M2–agarose affinity gel (Sigma–Aldrich) using 40  $\mu\text{l}$  per 10 mg of total proteins. Immunocomplexes were eluted from the anti-FLAG affinity gel using 1  $\mu\text{l}$  of elution buffer [immunoprecipitation buffer A with 200  $\mu\text{g}/\text{ml}$  3X-FLAG peptide (Sigma–Aldrich)] per  $\mu\text{l}$  of gel. For the immunoprecipitation assays using specific antibodies directed against endogenous interactors, lysates either from transfected HEK-293 or 697 cells were incubated overnight at 4°C with 1–3  $\mu\text{g}$  of a specific antibody, i.e. anti-MED7, anti-CRSP3, anti-CDK9, anti-ELL, anti-YWHAQ, anti-YWHAE or anti-SIAH-1 and, only for lysate from 697 cells, anti-AF4 antibody for immunoprecipitation, per 10 mg of total proteins. Subsequently, the mixture from HEK-297 cells was incubated with 30  $\mu\text{l}$  of Protein A/G PLUS–agarose (Santa Cruz Biotechnology) per 1  $\mu\text{g}$  of antibody, and the immunocomplexes were washed several times with immunoprecipitation buffer A. Otherwise, the mixture from 697 cells was incubated with 5  $\mu\text{l}$  of Protein A–Sepharose 4 Fast Flow (GE Healthcare) per 1  $\mu\text{g}$  of antibody, and the Sepharose-bound immunocomplexes were washed several times with immunoprecipitation buffer B. As a negative control, we used cell extracts incubated with serum IgGs (goat or rabbit, Sigma–Aldrich), processed in a similar manner to the samples.

### Western blot analysis

Either 40  $\mu\text{g}$  of WCE (whole-cell extract) from HEK-293 cells, or 40  $\mu\text{g}$  of WCE from 697 cells, or 15  $\mu\text{l}$  of sample

from each immunoprecipitation experiment were loaded on to SDS/PAGE and then transferred on to a nitrocellulose membrane for Western blot analysis. Blots were incubated with the following primary antibodies: anti-FLAG-M2 (1:5000 dilution) or anti- $\alpha$ -tubulin (1:1000 dilution); anti-AF4 for Western blotting (1:8000 dilution); anti-CDK9, anti-YWHAQ, anti-YWHAE, anti-SIAH-1 (all at a 1:1000 dilution); anti-ELL (1:500 dilution); anti-MED1, anti-MED7, anti-CRSP3, anti-MED27, anti-MED24, anti-MED17, anti-MED6 and anti-MED26 (all at a 1:200 dilution). Membranes were then incubated with HRP (horseradish peroxidase)-conjugated appropriate secondary antibodies, i.e. anti-mouse or anti-rabbit (1:5000 dilution) or anti-goat (1:8000 dilution). The bands were visualized with the ECL (enhanced chemiluminescence) or ECL Plus detection system (GE Healthcare).

### Preparative immunoaffinity purification

AF4-1-interacting proteins were purified using anti-FLAG-M2 affinity gel (Sigma-Aldrich) (as described above) on 50 mg of WCE from HEK-293 cells transfected with the FLAG-AF4-1 construct. The same purification protocol was also carried out with an equal amount of extract from HEK-293 cells that were transfected with the empty p3X-FLAG vector (mock control). The proteins eluted from the agarose beads were chloroform/methanol-precipitated and the pellets were dried [17].

### SDS/PAGE, in-gel digestion and MS analysis

The protein pellets obtained by affinity purification from transfected and from mock control cells were resuspended in SDS/PAGE buffer and fractionated by SDS/PAGE (10% gels). Protein electrophoretic patterns were visualized using Gel Code Blue Stain Reagent (Pierce). The two gel lanes were cut to generate 38 slices (~2 mm) per lane. Subsequent in-gel digestion and nano-LC-ESI (liquid chromatography-electrospray ionization)-MS/MS (tandem MS) analyses of each of the protein slices was performed as described previously [18,19].

Raw data from nano-LC-ESI-MS/MS analyses were converted into a peak list by using LC-MSD Trap 6.0 Build 485.0 (Agilent Technologies) to create a Mascot format text. Proteins were identified in-house by means of Mascot software version 2.1 (Matrix Science) [20]. The protein search was governed by the following parameters: non-redundant protein sequence data base (NCBI, July 2009 – 20070908 database with 7415798 sequences and 2558340887 residues downloaded; Sprout, July 2009 – 57.6 database with 495880 sequences and 174780353 residues downloaded); the protein sequence entries actually searched numbered 187996 for NCBI and 20331 for Sprout because of the taxonomy restriction to *Homo sapiens*; specificity of the proteolytic enzyme used for hydrolysis (trypsin); taxonomic category of the sample (*H. sapiens*); no protein molecular mass was considered; up to one missed cleavage; carbamidomethyl cysteine was set as a fixed modification, and protein N-acetylation, N-terminal pyroglutamate, oxidized methionine residues, and phosphorylation of serine, threonine or tyrosine were set as variable modifications; a precursor peptide maximum mass tolerance of 100 p.p.m. and a maximum fragment mass tolerance of 150 p.p.m. According to the probability-based Mowse score [20], the ion score is  $-10 \times \log(P)$ , where P is the probability that the observed match is a random event. Individual scores  $> 38$  indicate identity or extensive homology ( $P < 0.05$ ). Individual MS/MS spectra for peptides with a Mascot score equal to 38 were inspected manually. All of the peptides were inspected

for redundancy and represent sequences that are unique within the database used. Phosphopeptide spectra with a minimum Mascot score of 38 ( $P < 0.05$ ) were considered for further manual data interpretation. Phosphorylation site assignments by Mascot were validated and verified manually using the MS-Product tool (University of California San Francisco, Mass Spectrometry Facility, <http://prospector.ucsf.edu/>) with loss of  $H_3PO_4$  and multiple losses enabled as an additional option, focusing on the occurrence of b- and y-ions, internal fragments, and neutral losses of  $H_2O$ ,  $NH_3$  or  $H_3PO_4$  from these ions and the parent ion respectively.

### In silico analysis

To define an *in silico* 'interactome' map of AF4, we screened the HPRD (Human Protein Reference Database; freely available at <http://www.hprd.org>) for AF4 interactions [21]. We created a list of the known protein-protein interactions of AF4, and a list of primary (direct) and secondary (indirect) interactions was reported for each identified protein. In April 2011, the HPRD database contained 30047 human protein entries, 39194 protein-protein interactions and 453521 PubMed links. We used the HPRD, the BIND (Biomolecular Interaction Network Database; <http://bond.unleashedinformatics.com/Action>), DAVID bioinformatics resources (<http://www.david.abcc.ncifcrf.gov>) and STRING (<http://string.embl.de>) for protein clustering.

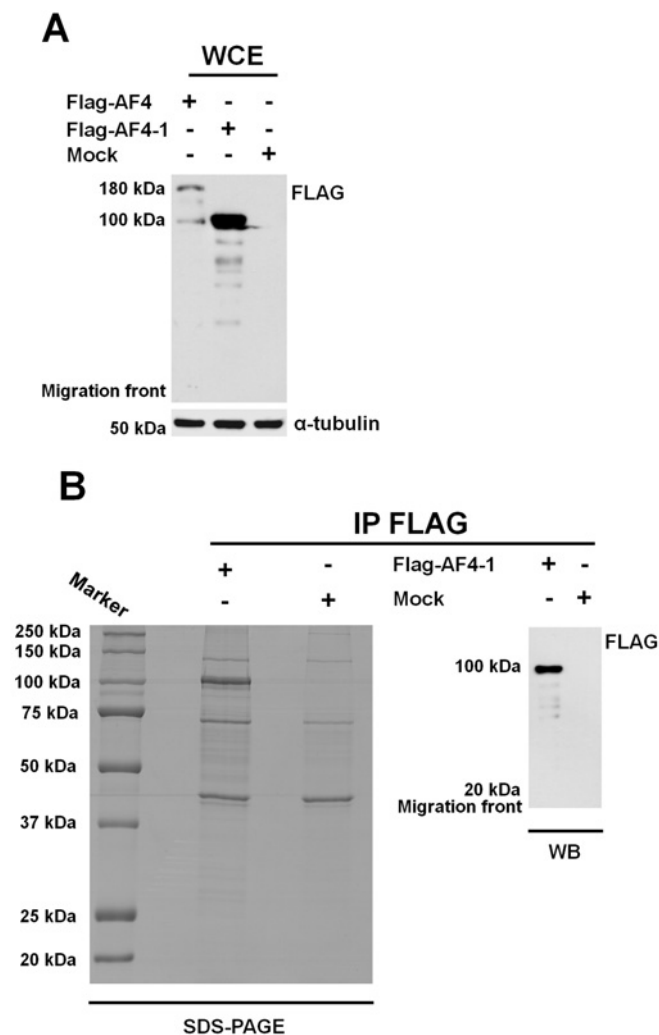
### Supporting information available (<http://www.BiochemJ.org/bj/438/bj4380121add.htm>)

Identification of AF4-1-interacting proteins by nanoLC/ESI-MS/MS, along with identified peptide sequences, precursor mass, charge state, mass errors, single peptide MASCOT score and sequence coverage (Supplementary Table S1). Analysis of control lane by nanoLC/ESI-MS/MS, along with identified peptide sequences, precursor mass, charge state, mass errors, single peptide MASCOT score, sequence coverage (Supplementary Table S2). Confirmation of identified phosphorylation sites (Supplementary Table S3). *In silico* analysis of AF4 interactors by the Human Protein Reference Database (<http://www.hprd.org>) (Supplementary Table S4).

## RESULTS AND DISCUSSION

We have used a functional proteomics approach to identify, in the HEK-293 cell line, proteins that interact with AF4, a member of the ALF family that supplies most of the partners of the oncogenic fusion proteins involved in childhood acute lymphoblastic leukaemia [1]. The present study represents one of the first global functional proteomic analyses to determine the identity of proteins that form a multimeric complex with AF4.

In contrast with HeLa, SAOS, K562 and SK-NB-E cell lines, the human HEK-293 cell line efficiently expressed our 'baits', the recombinant proteins FLAG-AF4-1 and FLAG-AF4 (Figure 1). Moreover, as reported in the HPRD and Unigene databases, the AF4 transcript is expressed in kidney, and HEK-293 cells have served previously as a heterologous expression system to study mouse recombinant AF4 [15]. We transfected HEK-293 cells with the full-length AF4 and with the AF4-1 cDNA constructs (Figure 2A). Co-immunoprecipitation with the flagged full-length AF4 protein yielded protein amounts that were sufficient for Western blot analysis, but not for an exhaustive functional proteomic analysis. Consequently, we used the FLAG-AF4-1 construct for large-scale immunoaffinity purification, and then validated the results in Western blot experiments with the



**Figure 2** Expression of flagged proteins and affinity co-immunoprecipitations

(A) Western blot analysis of recombinant AF4 polypeptides expressed in WCE from HEK-293 cells. An extract from cells transfected with the empty 3X-FLAG vector was used as a mock control. (B) Proteins from total lysate of HEK-293 cells transfected with FLAG-AF4-1 were immunoprecipitated using anti-FLAG agarose beads (IP FLAG). The FLAG-AF4-1 immunocomplex was in part separated by SDS/PAGE (10% gel) (left-hand panel, colloidal Coomassie Blue staining) and in part immunoblotted with an anti-FLAG monoclonal antibody (right-hand panel). In both cases, an immunoprecipitate from cells transfected with empty 3X-FLAG vector was used as a mock control. The molecular mass in kDa is indicated on the left-hand side. IP, immunoprecipitation; WB, Western blot.

full-length recombinant protein. It is of note that FLAG-AF4-1 encodes the N-terminal half of the protein containing the transactivation domain (Figure 1), but not the binding domains for AF9 and ENL, the other two most common MLL fusion partners [22].

Proteins from total lysates of HEK-293 cells transfected with FLAG-AF4-1 and with the empty vector (mock control) were immunoprecipitated, and immunocomplexes were fractionated by SDS/PAGE (10% gels) (Figure 2B). From each gel lane, we obtained 38 peptide mixtures, each of which was analysed in duplicate by MS. Peptide mixtures from the control lane were always injected before peptides from the sample lane to avoid carry-over.

Our analysis, although unable to distinguish between direct and indirect interactors, revealed 51 proteins, most of which

were not previously known to be molecular partners of AF4. They are listed in Table 1, grouped according to their function. Supplementary Table S1 (at <http://www.BiochemJ.org/bj/438/bj4380121add.htm>) shows, for each protein entry, the peptide sequence identified, the precursor mass ( $m/z$ ), the charge state ( $z$ ), the mass errors (p.p.m.) on the precursor peptide, the Mascot score for each peptide and the protein sequence coverage. Each protein is reported only with the gene symbol from NCBI source to eliminate redundancy.

To select proteins that specifically interact with AF4-1, we subtracted species that were common to AF4-1 and non-transfected control lanes (Figure 2B). These common proteins are shown in Supplementary Table S2 (at <http://www.BiochemJ.org/bj/438/bj4380121add.htm>). All protein species identified by a single peptide were checked further. First, the peptide sequence stretch was manually reconstructed, and then the peptide sequence and the peptide precursor ion mass were inserted into the Mascot software using the sequence query mode. All searches were performed against the NCBI nr and Sprot databases. The peptide sequence was searched for using BLAST software (<http://ncbi.nlm.nih.gov/blast>). Supplementary Table S1 shows the full MS scan and the properly annotated MS/MS scan (with masses and fragment assignments) of proteins identified by a single peptide.

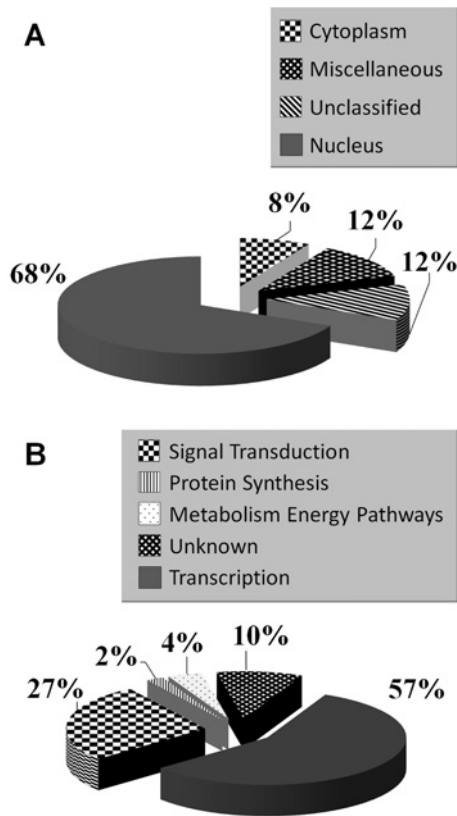
We classified the human proteins identified according to their Gene Ontology cellular localization (Figure 3A) and to the biological processes in which they are involved (Figure 3B). It is of note that the nature of the identified proteins, which are mainly localized in the nucleus (68%), points to the existence of a large protein network involving AF4. Approximately 60% of the proteins identified that take part in this cross-talk are clustered in the Pol II transcriptional complex.

To check the authenticity of the AF4-interacting proteins identified by MS/MS, we verified the presence of some of these proteins by anti-FLAG co-immunoprecipitation and Western blot analysis, depending on the availability and efficiency of commercial antibodies. We confirmed that CRSP3/MED23, ELL, CDK9, CRSP3/MED7, YWHAQ and YWHAE specifically interact with AF4-1 and with the full-length AF4 (Figure 4A), thus demonstrating that the latter two, despite their difference in length, have similar folding in common regions. We also identified SLAH-1, a known molecular direct interactor of AF4 [10,11] (Figure 4A). We validated the AF4 interactors further by reverse immunoprecipitation experiments using specific anti-CDK9, anti-YWHAQ, anti-CRSP3, anti-MED7, anti-ELL and anti-YWHAE antibodies on extracts from HEK-293 cells transfected with FLAG-AF4. Western blot analysis with the anti-FLAG antibody revealed the FLAG-tagged protein in each immunocomplex (Figure 4B). These interactions were also confirmed by Western blot analysis of immunocomplexes obtained from protein extracts of an haemopoietic cell line, the human pre-B lineage leukaemia 697 cells, by using specific antibodies directed against either endogenous AF4 or endogenous interactors (Figure 5). Overall, our immunoprecipitation experiments support the conclusion that endogenous CDK9, YWHAQ, CRSP3/MED23, CRSP3/MED7, ELL and YWHAE interact with FLAG-AF4 in HEK-293 cells, but they also interact with endogenous AF4 in 697 leukaemia cells.

We also tested antibodies directed against all of the components of the mediator complex that we identified in our proteomic study, namely CRSP8/MED27, THRAP4/MED24, PPARBP/MED1, CRSP6/MED17, MED6 and CRSP7/MED26. However, these antibodies failed to detect the respective target proteins in cellular extracts from HEK-293, HeLa, SAOS, SK-NB-E, K562 or 697 cells analysed by Western blotting (results not shown).

**Table 1 AF4-1-interacting proteins identified by nano-LC-ESI-MS/MS and their Gene Ontology classification**

Gene symbol	Accession number	Protein
Transcription-regulatory proteins		
<i>PPARBP, MED1</i>	gij2765322	Activator-recruited cofactor 205 kDa component
<i>MED12</i>	gij4827042	Mediator of RNA polymerase II transcription, subunit 12 homologue
<i>CRSP2, MED14</i>	gij4580326	Cofactor required for Sp1 transcriptional activation, subunit 2, 150 kDa
<i>CRSP3, MED23</i>	gij28558969	Cofactor required for Sp1 transcriptional activation, subunit 3, 130 kDa
<i>THRPA4, MED24</i>	gij8699628	Vitamin D receptor-interacting protein complex component DRIP100
<i>CRSP6, MED17</i>	gij28558975	Cofactor required for Sp1 transcriptional activation, subunit 6, 77 kDa
<i>CRSP7, MED26</i>	gij28558977	Cofactor required for Sp1 transcriptional activation, subunit 7, 70 kDa
<i>RBBP4</i>	gij13111851	Retinoblastoma-binding protein 4
<i>RUVBL2</i>	gij13111851	48 kDa TATA-box-binding protein-interacting protein
<i>EAF1</i>	gij27370592	ELL-associated factor 1
<i>MED4</i>	gij7141320	p36 TRAP/SMCC/PC2 subunit (Mediator of RNA Pol II transcription, subunit 4 homologue)
<i>CRSP8, MED27</i>	gij7141322	Cofactor required for Sp1 transcriptional activation, subunit 8, 34 kDa
<i>MED7</i>	gij13528909	Cofactor required for Sp1 transcriptional activation, subunit 9
<i>MED6</i>	gij3329506	RNA polymerase transcriptional regulation mediator
<i>MED8</i>	gij33988564	Mediator of RNA polymerase II transcription subunit 8 activator-recruited cofactor 32 kDa component
<i>TRFP, MED20</i>	gij4323033	Trf (TATA binding protein-related factor)-proximal homologue
<i>MED21</i>	gij1515377	RNA polymerase II holoenzyme component SRB7
<i>ELL</i>	gij10130023	RNA polymerase II elongation factor ELL
<i>PCQAP</i>	gij14043091	MED15
<i>TCEA1</i>	gij313223	Transcription elongation factor A (SII), 1
DNA-directed RNA polymerase proteins		
<i>POLR2A</i>	gij36124	RNA polymerase II largest subunit
<i>POLR2B</i>	gij4505941	RNA polymerase II second largest subunit
<i>POLR2C</i>	gij2920711	Polymerase (RNA) II (DNA-directed) polypeptide C, 33kDa
DNA-binding proteins		
<i>MCM3</i>	gij1552242	DNA polymerase $\alpha$ -holoenzyme-associated protein P1 (p102 protein)
<i>RUVBL1</i>	gij15277588	49 kDa TATA box-binding protein-interacting protein
RNA-binding proteins		
<i>NCL</i>	gij189306	Nucleolin
<i>PRPF31</i>	gij40254869	PRP31 pre-mRNA processing factor 31 homologue
<i>SNRPD2</i>	gij29294624	Small nuclear ribonucleoprotein D2 polypeptide 16.5 kDa
Serine/threonine kinase protein		
<i>CDK9</i>	gij12805029	Cyclin-dependent kinase 9 (CDC2-related kinase)
Serine/threonine phosphatase protein		
<i>PPP2R1A</i>	gij178663	Protein phosphatase 2 (formerly 2A) regulatory subunit A (PR 65) $\alpha$ isoform
Translation regulator protein		
<i>EEF1B2</i>	gij12652911	Eukaryotic translation elongation factor 1 $\beta$ 1
Auxiliary transport protein		
<i>GDI2</i>	gij285975	Rab GDP dissociation inhibitor $\beta$
Receptor signalling complex scaffold proteins		
<i>YWHAE</i>	gij12655169	14-3-3 protein, $\epsilon$ isoform (protein kinase C inhibitor protein 1)
<i>YWHAQ</i>	gij55594676	14-3-3 protein $\theta$ (14-3-3 protein T-cell)
<i>SPIN</i>	gij5730065	SPINL
<i>AP3S1</i>	gij4502861	Adapter-related protein complex 3 $\sigma$ 1 subunit
Signal transduction proteins		
<i>CCNT1</i>	gij2981196	CDK9 associated C-type cyclin
<i>S100A8</i>	gij21614544	S100 calcium-binding protein A8
<i>S100A9</i>	gij4506773	S100 calcium-binding protein A9
Transmembrane receptor protein tyrosine kinase protein		
<i>FGFR2</i>	gij29432	Fibroblast growth factor (FGR) receptor
Lipid kinase proteins		
<i>PIP5K2B</i>	gij1857637	Phosphatidylinositol-4-phosphate 5-kinase type II, $\beta$
<i>PIP5K2C</i>	gij21322230	Phosphatidylinositol-4-phosphate 5-kinase, type II, $\gamma$
Heterotrimeric G-protein GTPase protein		
<i>GNB4</i>	gij12654119	Guanine-nucleotide-binding protein (G-protein), $\beta$ polypeptide 4
Guanyl-nucleotide exchange factor protein		
<i>ARRHGEF4</i>	gij8809845	Rho guanine-nucleotide-exchange factor (GEF) 4
Enzyme: dehydrogenase		
<i>GAPDH</i>	gij31645	Glyceraldehyde-3-phosphate dehydrogenase
Enzyme: synthase		
<i>PTS</i>	gij4506331	6-pyruvoyltetrahydropterin synthase
Unknown		
<i>SMAD9</i>	gij13959539	MAD mothers against decapentaplegic homologue 9
<i>LSM14A</i>	gij16877144	LSM14 homologue A (RNA-associated protein 55)
<i>DRG1</i>	gij17939479	Developmentally regulated GTP-binding protein 1 (neural precursor cell expressed developmentally down-regulated 3)
<i>HCCA2</i>	gij55249549	HCCA2 protein (MOB2)
<i>C20orf11</i>	gij21594655	Chromosome 20 open reading frame 11



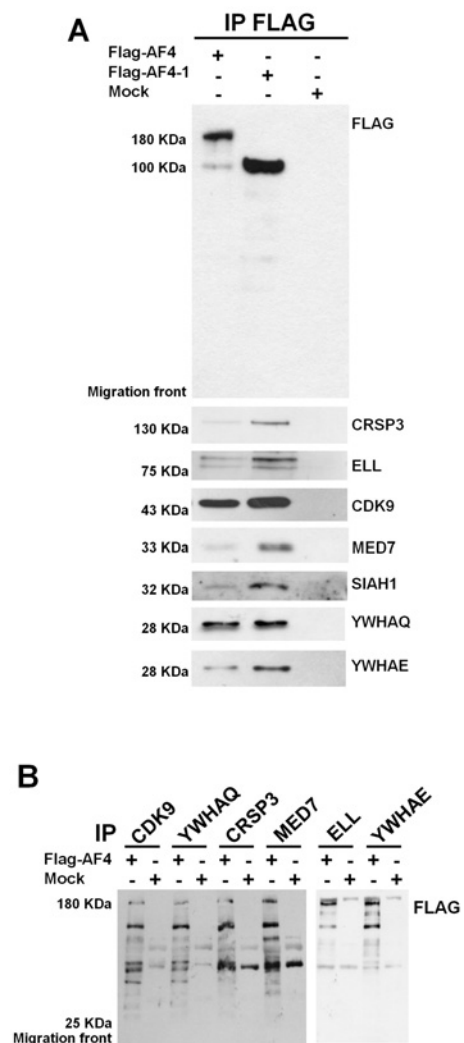
**Figure 3** Classification of the identified proteins

(A) According to Gene Ontology Cellular Localization and (B) Biological Processes.

It is of note that in our system we did not identify all of the proteins previously reported to interact with AF4. This is probably due to the use of the N-terminal half of AF4 as 'bait'. In fact, we did not find AF9, ENL, DOT1L or AF5q31, the AF4 partners known to interact with its C-terminal half [23]. However, although our bait (FLAG-AF4-1) lacks the crucial C-terminal-binding domain, we were able to identify various known and new molecular partners, thereby providing further insight into AF4 function in normal and leukaemic conditions. Obviously we cannot exclude that some of the reported interactions may be cell-lineage specific; however, almost all of the proteins that form the AF4 interactome, as well as AF4 itself, are variably expressed in various cell types, according to the UniGene database (<http://www.ncbi.nlm.nih.gov/uniGene>).

AF4 is a phosphorylated protein [15], but its phosphorylation sites are still unknown. LC-MS/MS analysis of the bait protein revealed two phosphorylation sites (Figure 2B). The MS2 spectra from the identified phosphopeptides are shown in Figure 6. Peptide ELSPLISLPSPVPLSPIHSNQQTLPR turned out to be phosphorylated on Thr<sup>220</sup> and Ser<sup>212</sup> (Figures 6A and 6B respectively). We also identified the corresponding unmodified peptide (Figure 6C). The phosphorylation sites identified were manually confirmed (Supplementary Figure S1 at <http://www.BiochemJ.org/bj/438/bj4380121add.htm>). Although this peptide was previously reported to be phosphorylated [24], we indicate for the first time the precise localization of the phosphorylation sites.

To extend our data, we carried out an *in silico* proteomic analysis of proteins that are known to directly or indirectly interact with AF4. Examination of the HPRD indicated two

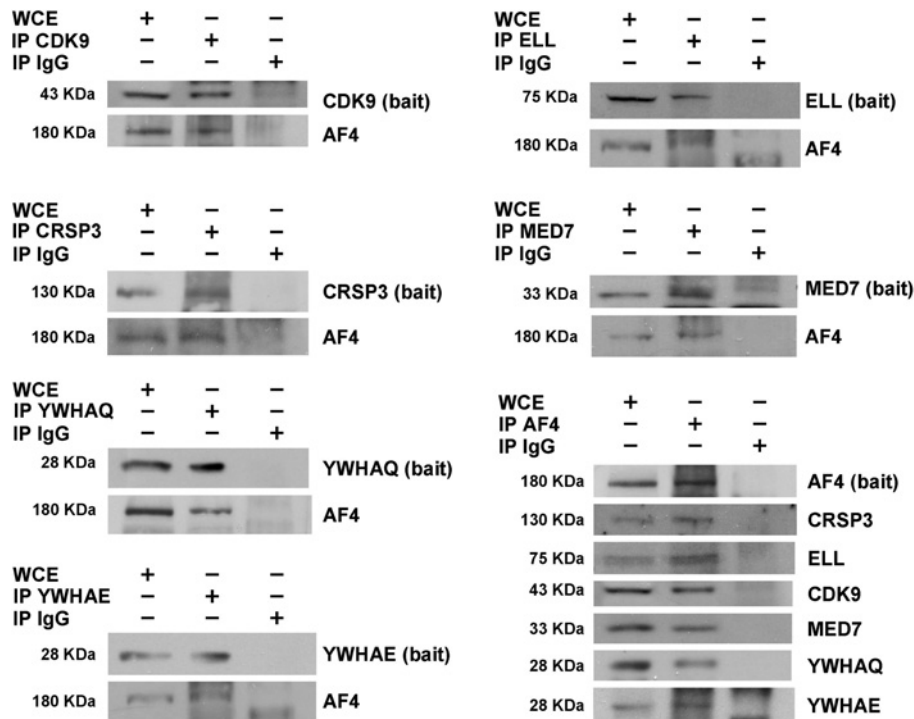


**Figure 4** FLAG-AF4 associates with CRSP3, MED7, ELL, CDK9, SIAH1, YWHAQ and YWHAЕ

(A) Proteins from total lysate of HEK-293 cell lines transfected respectively with FLAG-AF4, FLAG-AF4-1 and empty vector (mock control) were immunoprecipitated using anti-FLAG agarose beads, then resolved by SDS/PAGE (10% gel) and analysed by Western blotting with specific antibodies. (B) Proteins from WCE of HEK-293 cells transfected respectively with FLAG-AF4 and empty vector (mock control) were immunoprecipitated using specific antibodies, then resolved by SDS/PAGE (8% gel) and analysed by Western blotting with an anti-FLAG antibody. The molecular mass in kDa is indicated on the left-hand side. IP, immunoprecipitation.

direct interactions for AF4: SMAD9 and ENL [23,25]. In the present study, we identified SMAD9, also known as SMAD8A or SMAD8B (Table 1 and Supplementary Table S1). We carried out a detailed clustering analysis using the HPRD to look for a protein network involved in the same functional scenario. To this aim, we filled out a comprehensive list of known primary and secondary interactions for all proteins found in the present study (see Supplementary Table S3 at <http://www.BiochemJ.org/bj/438/bj4380121add.htm>).

Several proteins reported in the present study interact with each other, thus suggesting that they participate in the same multiprotein complex or complexes. The vast majority of proteins interacting with human AF4 are involved in Pol II-mediated transcription. Thus there is compelling evidence that AF4 plays a key role in the Pol II transcription machinery. Figure 7 shows a



**Figure 5** Endogenous AF4 associates with CRSP3, MED7, ELL, CDK9, SIAH1, YWHAQ and YWHAE

Proteins from total lysates of 697 cell lines were immunoprecipitated (IP) using anti-AF4, anti-CDK9, anti-YWHAQ, anti-CRSP3, anti-MED7, anti-ELL and anti-YWHAE antibodies. Immunocomplexes were resolved by SDS/PAGE (10% gel) and analysed by Western blotting with specific antibodies. WCE represents the control and IgG the mock. The molecular mass in kDa is indicated on the left-hand side.

map of the AF4-interacting proteins, with Pol II as the core of the interactions.

Indeed, our proteomics analysis identified the serine/threonine kinase CDK9 and cyclin T1 (CCNT1) that interact each other and form the positive transcription elongation factor P-TEFb, which activate the Pol II elongation machinery [26]. It is known that AF4 associates with P-TEFb, positively regulates its kinase activity and stimulates Pol II transcriptional elongation [15]. Through its ability to phosphorylate the Pol II CTD (C-terminal domain), P-TEFb controls productive elongation of most eukaryotic genes, but also co-ordinates downstream events including pre-mRNA splicing and 3'-end processing [27]. P-TEFb recruits various positive regulators other than AF4, namely, the transcriptional activators HIV Tat, CIITA, c-Myc, NF- $\kappa$ B (nuclear factor  $\kappa$ B), MyoD, Brd4, AF5q31 and ELL to specific gene promoters and stimulates transcriptional elongation [16,26,28,29]. A recent paper demonstrate that AF4, AF5q31 and ENL associate in an endogenous higher-order complex containing P-TEFb in haemopoietic lineage cells [16]. Our results indicate that such a complex should also be formed in HEK-293 cells. Therefore we mapped the CDK9-binding region along AF4. To this aim, we produced three new flagged constructs, namely AF4-1.1 (bp 4–833), AF4-1.2 (bp 696–1497) and AF4-1.3 (bp 1384–1950) (Figure 1), which we used to transiently transfect HEK-293 cells. We analysed the corresponding anti-FLAG immunoprecipitates by Western blotting with the anti-CDK9 antibody (Figure 8) and found that, in agreement with Yokoyama et al. [16], only AF4-1.1 (aa 2–277) was able to interact with CDK9. Intriguingly, this peptide contains Ser<sup>212</sup> and Thr<sup>220</sup>, which we found to be phosphorylated in our structural characterization of AF4.

P-TEFb phosphorylates AF4 and down-regulates its transactivation activity [15]. Therefore phosphorylation is a key

control mechanism of AF4 activity, and the AF4 N-terminal region might reasonably be the P-TEFb phosphorylation site. This type of control should thus be ineffective on MLL–AF4 chimaeras that lack the AF4 N-terminus. It is notable that, phosphorylation events regulate the function of other components that we identified in the AF4 protein network [e.g. 14-3-3 proteins, FGFR2 (fibroblast growth factor receptor 2), Pol II, nucleolin and MCM (minichromosome maintenance)].

In eukaryotes, Pol II is the central component of the basal Pol II transcription machinery. It moves on the template as the transcript elongates [30]. Elongation is influenced by the P-TEFb-mediated phosphorylation of the CTD of the largest Pol II subunit [31]. In agreement with our present study and with reports from other groups showing that AF4 directly interacts with P-TEFb [15,16], we identified in the AF4 multiprotein complex, the largest subunit (POLR2A), the second largest subunit (POLR2B) and a small subunit of 33 kDa (POLR2C) of Pol II. In addition, we found: (i) nucleolin, which forms complexes with POLR2A, CDK9 and CCNT1, and plays a role in transcriptional elongation [32]; (ii) TCEA1 (transcription elongation factor A), another Pol II transcription elongation factor, which has a role in suppression of transient pausing and strongly synergizes with p300 histone acetylase at a step subsequent to pre-initiation complex formation [33]; and (iii) MCMs, a family of proteins related to ATP-dependent helicases, which has been co-purified with Pol II after anti-MCM3 immunoaffinity chromatography [34]. The results of the present study support the idea that MCM proteins are components of the Pol II transcriptional apparatus [34].

We also found that AF4-1 interacts with the Pol II elongation factor ELL that, as well as AF4, ENL and AF5q31, is frequently fused to MLL in childhood lymphoblastic leukaemia [34]. ELL is a multifunction factor that exerts transcriptional elongation

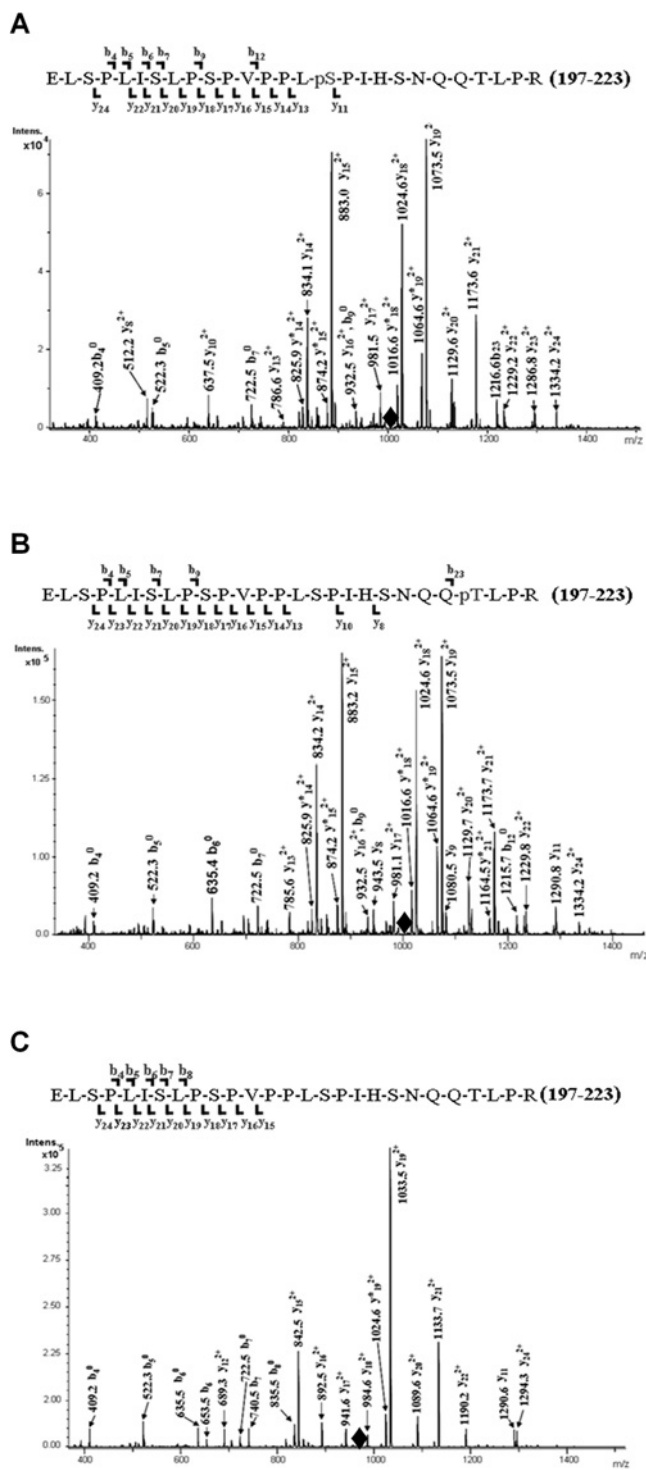


Figure 6 MS/MS spectra of modified and unmodified peptides of AF4

(A) MS/MS spectrum of ELSPLSLPSPVPLSPPIHSNQQLPLR; (B) MS/MS spectrum of ELSPLSLPSPVPLSPPIHSNQQLPLR; (C) MS/MS spectrum of ELSPLSLPSPVPLSPPIHSNQQLPLR. ◆ indicates the  $m/z$  signal of the parent ion.

activity and inhibitory effects on the initiation of Pol II-mediated transcription [35,36], besides acting as a transcription factor [37]. In particular, the CTD of ELL interacts with P-TEFb [36], a molecular interactor of the N-terminal domain of AF4, as we demonstrate in the present study. Our proteomic analysis also identified EAF1 (ELL-associated factor 1) [38]. EAF1

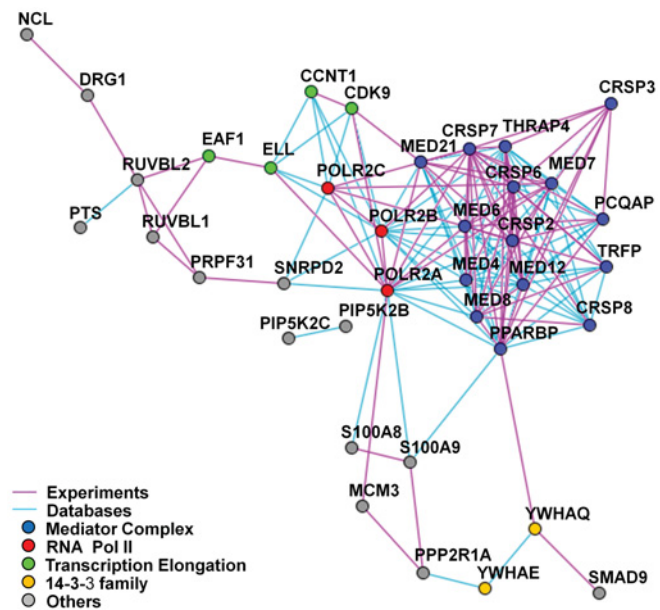


Figure 7 Map of protein–protein interactions

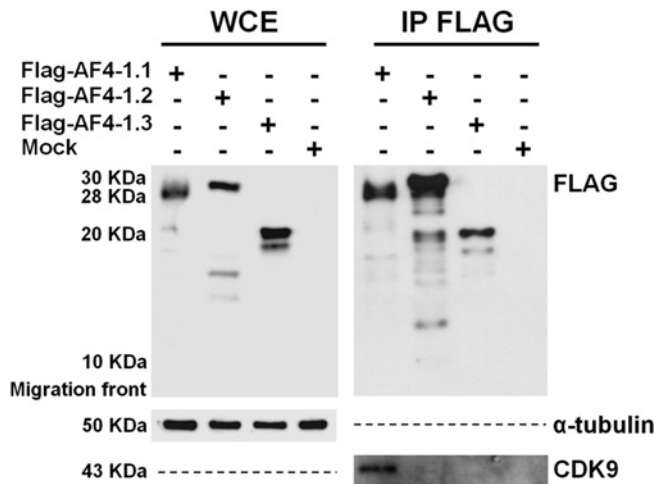
All proteins identified in the present study are reported in the map that was obtained using the open-source software STRING. AF4 protein is not included. The purple lines indicates interactions proved by *in vitro* and/or *in vivo* assay and previously reported in the literature (PubMed); the blue lines show proteins that participate in the same complex, as reported in the well-annotated databases HPRD, Database of Interacting Proteins (DIP) and BioGrid (<http://www.thebiogrid.org/>). The physical distance between two proteins (nodes) along an edge in a graph has no meaning.

interaction with the CTD of ELL is necessary and sufficient for the leukaemogenic effect of the MLL–ELL fusion protein [38]. Notably, a heterologous MLL–EAF1 fusion protein recapitulates the phenotype of MLL–ELL *in vitro* and *in vivo* [38]. EAF1 is a strong positive regulator of ELL elongation activity and contains a transactivation domain that has high sequence identity with the transactivation domain of AF4 [38]. Therefore it is not surprising that the latter may also associate with ELL and positively regulate its transactivating function [38,39]. The identification of ELL and EAF1 among AF4 interactors is in line with a recent report demonstrating that ELL and EAF1 are part of a SEC (super elongation complex), which includes P-TEFb, AF5q31, ENL and AF4, that is crucial in the control of transcription elongation [40]. Such a complex should be recruited constitutively by MLL chimaeras that should thus be able to bypass the normal transcription initiation and elongation checkpoint steps, and activate aberrant MLL-target gene expression [16,40]. Indeed, knockdown of the central SEC component AF5q31 in MLL–AF4 leukaemia cells causes a reduction in the expression of *HOXA9*, a key mediator of leukaemogenesis [40].

Although we cannot be sure about the interactions that were not validated with immunoprecipitation/Western blot methods, the data discussed so far demonstrate the appropriateness of our proteomic approach. In fact, all the interactions we identified are in line with the most recent findings about the composition of the multiprotein complex involving AF4 [16,40]. Indeed, the finding of Pol II subunits in this complex supports the crucial role of AF4 in the transcriptional machinery. However, the novelty of the present study resides in the identification of 15 out of the 28 proteins that form the mammalian Mediator complex (Table 1).

The Mediator complex is a multiprotein transcription factor that is evolutionarily conserved and ubiquitously expressed in eukaryotes from yeast to man [41,42]. This large multisubunit





**Figure 8** CDK9 interacts with the N-terminal region of AF4 (aa 2–277)

Proteins from total lysate (WCE) of HEK-293 cell lines transfected respectively with three constructs coding for different regions of AF4-1 fragment (see Figure 1) and with empty vector (mock control) were immunoprecipitated (IP) using anti-FLAG antibodies, resolved by SDS/PAGE (12% gel) and analysed by Western blotting with an anti-CDK9 antibody. The molecular mass in kDa is indicated in the left-hand side.

complex is the primary regulator of the assembly of the pre-initiation complex, which includes the general transcription factors TFIIA, TFIIB, TFIID, TFII E, TFII F, TFII E and Pol II [41–43]. In general, transcription factors and activators physically bind to a specific subunit of Mediator and thereby recruit other components of the complex to the target promoter. In particular, activator binding provokes specific conformational shifts in Mediator that induce a conformational state in the neighbouring subunits of the complex. Indeed, Mediator can adopt various conformations after the binding of different transcriptional activators to different Mediator subunits [44]. Therefore structural changes in Mediator afford additional opportunities to fine-tune the diverse regulatory inputs received from the DNA-binding factors and from other signals to the transcription machinery [45]. Genetic, biochemical and structural data revealed that Mediator comprises several modules (head, middle, tail and CDK8) [46]. The head, middle and tail modules form a relatively stable ‘core’ that is composed of 18–20 tightly associated subunits [40,45]. Otherwise, the subunits PPARBP/MED1, MED25 and MED8, and the module constituted by CRSP3/MED23, THRAP4/MED24 and TRAP95/MED16 are variably and weakly associated with the central core [40]. The constant core and the variably associated proteins are considered to be components of the active forms of the Mediator complex. In contrast, SRB10/CDK8, MED13, MED12 and SRB11/CycC (cyclin C) form a functional and physically separable module that has been implicated in transcriptional repression [40,45]. The potential microheterogeneity could result in a wide spectrum of mammalian Mediator complexes [47].

Our proteomic analysis of the AF4 complex identified ten Mediator central core subunits (TRAP36/MED4, TRAP32/MED6, CRSP33/MED7, CRSP2/MED14, CRSP6/MED17, TRFP/MED20, MED21, CRSP7/MED26, PCQAP/MED15 and CRSP8/MED27) and four variable subunits (PPARBP/MED1, MED8, CRSP3/MED23 and THRAP4/MED24). Apart from MED12, all of the components identified belong to the active form of Mediator. It is of note, however, that MED12 directly interacts with mammalian  $\beta$ -catenin and activates target genes,

thus indicating that MED12 also has an alternative activating role [48]. Interestingly,  $\beta$ -catenin is activated during development of MLL leukaemic stem cells [49].

As our identifications indicate that AF4 interacts with Pol II and the Mediator complex, we may speculate that AF4 binding induces a structural change in Mediator thereby activating stalled Pol II to transition to a positively elongating state and enabling effective transcription to take place. Therefore the AF4–Mediator complex interaction might be crucial for activation of specific gene expression. In this context, it is of note that Yokoyama et al. [16] demonstrate that the AEP complex (AF4, AF5q31, ENL and P-TEFb) co-localizes with wild-type MLL on specific target promoters, thereby indicating that this complex plays a role in physiological as well as in oncogenic MLL-dependent transcriptional pathways. However, they also showed that recruitment of AEP to MLL-target loci was not constitutive, because some MLL-occupied loci (e.g. *HOXA7*) did not contain AEP. Therefore these authors hypothesized that the MLL complex probably requires other, as yet unidentified, factors or signals for specific recruitment of AEP, and concluded that AEP recruitment, a downstream event in physiological MLL-dependent transcriptional pathways, is regulated in a context-dependent manner. This hypothesis suggested that the results of the present study may be integrated into the Yokoyama et al. [16] model. Specifically, we suggest that the Mediator complex, depending on its subunit composition, plays a crucial role in the recruitment of the AEP complex on specific MLL-target promoters. Indeed, the wild-type MLL complex may initiate the activation pathway by binding the regulatory region of target genes. It would then recruit some specific Mediator components, in a context-dependent manner. For example, MLL could recruit the head subunit MED17/TRAP80, a known direct interactor of ASH2L [ash2 (absent, small, or homeotic)-like] that, together with RBBP4 (retinoblastoma binding protein 4), an AF4 partner (Supplementary Figure S1), forms the MLL complex [50,51]. Alternatively, some Mediator components may recruit MLL directly to the target chromatin. Indeed, PPARBP/MED1 directly interacts with various ligands of nuclear receptors (thyroid hormone receptor, vitamin D receptor, peroxisome proliferator-activated receptor- $\gamma$ , hepatocyte nuclear factor 4 $\alpha$ , glucocorticoid receptor and oestrogen receptor), as well as with non-receptor type factors such as GATA1 (GATA-binding protein 1). After these initial recruitments, assembly of the pre-initiation complex, which entails the various general transcription factors and Pol II, and transcription initiation then ensue, together with the concomitant recruitment of other ad hoc components of the Mediator complex. After Pol II clears the promoter, the process can proceed directly to the elongation phase thanks to the Mediator-dependent specific recruitment of AF4 and the other components of the AEP complex described by Yokoyama et al. [16].

Lastly, we found that YWHAQ and YWHA E, two members of the 14-3-3 protein family, interact with AF4. 14-3-3s are ubiquitous proteins, usually cytosolic, that exert an extraordinarily wide-ranging influence on cellular functions, including cell-cycle control and apoptosis. They operate by binding to specific phosphorylated sites on such diverse target proteins as oncogene products, tumour suppressor proteins, and regulators of cell survival, proliferation and growth [52]. 14-3-3s are often associated with dynamic nucleo-cytoplasmic shuttling. Upon phosphorylation, many nuclear proteins, including transcription factors, bind to 14-3-3s, which control their rate of nuclear import/export thereby modulating transcriptional processes [52]. We suggest that 14-3-3s bind phosphorylated AF4 and contribute to the regulation of its movement into and out of the nucleus.

In the cytosol, AF4 undergoes rapid proteasomal degradation via its well-known interaction with SIAH-1a and SIAH-2 ubiquitin ligases [10,11]. This mechanism could closely control AF4 turnover and, consequently, AF4-dependent transcriptional elongation. The phosphorylation sites that we have identified in AF4 might play a key role in the putative 14-3-3-mediated AF4 regulation/degradation pathway.

The characterization of AF4-interacting proteins reported in the present paper supports the growing body of evidence that AF4 is a crucial activator in a multimeric complex that promotes transcription in human cells, and that this multiprotein complex is functionally and structurally regulated (i.e. via the availability of components, phosphorylation, proteasome-mediated degradation, cellular localization and conformational shifts). Indeed, the results of the present study greatly increase the number of putative components participating in the multiprotein complex formed by AF4, as well as by other MLL fusion partners (ENL ELL, AF5q31, AF9 etc.). The information reported in the present paper is useful for future studies aimed at unravelling the AF4-dependent molecular mechanisms, thereby giving insights into the molecular basis of AF4-mediated leukaemia and eventually leading to novel therapeutic targets. We previously reported that even when MLL–AF4 chimaeras lack part of the AF4 transactivation domain, they continue to give rise to acute lymphoblastic leukaemia [53]. Given results from previous studies [16,40] and the results of the present study, it is now clear also that this altered MLL–AF4 chimaera, irrespective of the transactivation domain, is able to recruit all of the protein components that are necessary for the transcription of genes that enhance and sustain cell transformation.

#### Note added in press

While this article was being processed, a paper appeared [54] that contains some results that overlap our findings.

#### AUTHOR CONTRIBUTION

Gabriella Esposito participated in designing the experiments, provided conceptual input, collated all the data and wrote the final version of the manuscript. Armando Cevenini and Alessandro Cuomo designed and performed the experiments. Francesca De Falco and Dario Sabbatino participated in the design and execution of the experiments. Fabrizio Pane participated in the analysis and discussion of the results. Margherita Ruoppolo participated in designing the experiments and contributed to the discussion and interpretation of the data. Francesco Salvatore conceived the rationale of the investigation and the overall experimental design, participated in the analysis and discussion of the results and in writing the paper. All authors revised the manuscript, and gave their approval to the final version of the text.

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## SUPPLEMENTARY ONLINE DATA

# Protein network study of human AF4 reveals its central role in RNA Pol II-mediated transcription and in phosphorylation-dependent regulatory mechanisms

Gabriella ESPOSITO\*†, Armando CEVENINI\*†, Alessandro CUOMO\*, Francesca DE FALCO‡, Dario SABBATINO†, Fabrizio PANE\*†, Margherita RUOPPOLO\*† and Francesco SALVATORE\*‡<sup>1</sup>

\*CEINGE-Biotecnologie Avanzate, s.c.a r.l., Via G. Salvatore 486, 80145 Naples, Italy, †Dipartimento di Biochimica e Biotecnologie Mediche, Università di Napoli "Federico II", Via S. Pansini 5, 80131 Naples, Italy, and ‡IRCCS-Fondazione SDN, Via E. Gianturco 113, 80143 Naples, Italy

Figure S1 and Tables S1–S3 are on the pages that follow.

<sup>1</sup> To whom correspondence should be addressed (email salvator@unina.it).



# Mascot Search Results

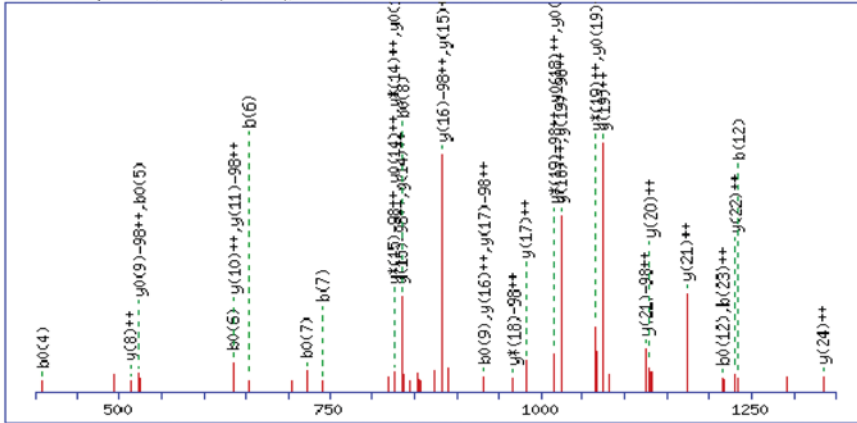
## Peptide View

MS/MS Fragmentation of **ELSPILSPSPVPLSPIHSNQQpTLPR**

Found in **IPI00396310**, Tax\_Id=9606 Gene\_Symbol=AFF1 AF4/FMR2 family, member 1

Match to Query 584: 2996.738172 from(999.920000,3+) intensity(1580476.0000)

Title: Cmpd 530, +MSn(1000.5), 23.7 min



The  $y_8^{2+}$  (512.2 m/z) and  $b_{23}$  (1216.6 m/z) ion fragments were ruled out phosphorylation at threonine 220 (The amino acid positions are referred to Swiss-Prot entry **P51825**)

Monoisotopic mass of neutral peptide Mr(calc): 2996.5736

Ions Score: 83 Expect: 2.4e-006

Matches (Bold Red): 41/422 fragment ions using 36 most intense peaks

#	b	b <sup>++</sup>	b <sup>*</sup>	b <sup>+++</sup>	b <sup>0</sup>	b <sup>0++</sup>	Seq.	y	y <sup>++</sup>	y <sup>*</sup>	y <sup>+++</sup>	y <sup>0</sup>	y <sup>0++</sup>	#
1	130.0499	65.5286			112.0393	56.5233	E							27
2	243.1339	122.0706			225.1234	113.0653	L	2868.538	1434.773	2851.512	1426.26	2850.528	1425.768	26
3	330.166	165.5866			312.1554	156.5813	S	2755.454	1378.231	2738.428	1369.718	2737.444	1369.226	25
4	427.2187	214.113			<b>409.2082</b>	205.1077	P	2668.422	<b>1334.715</b>	2651.396	1326.202	2650.412	1325.71	24
5	540.3028	270.655			<b>522.2922</b>	261.6498	L	2571.369	1286.188	2554.343	1277.675	2553.359	1277.183	23
6	<b>653.3869</b>	327.1971			<b>635.3763</b>	318.1918	I	2458.285	<b>1229.646</b>	2441.259	1221.133	2440.275	1220.641	22
7	<b>740.4189</b>	370.7131			<b>722.4083</b>	361.7078	S	2345.201	<b>1173.104</b>	2328.175	1164.591	2327.191	1164.099	21
8	853.5029	427.2551			<b>835.4924</b>	418.2498	L	2258.169	<b>1129.588</b>	2241.143	1121.075	2240.159	1120.583	20
9	950.5557	475.7815			<b>932.5451</b>	466.7762	P	2145.085	<b>1073.046</b>	2128.059	<b>1064.533</b>	2127.075	<b>1064.041</b>	19
10	1037.588	519.2975			1019.577	510.2922	S	2048.033	<b>1024.52</b>	2031.006	<b>1016.007</b>	2030.022	<b>1015.515</b>	18
11	1134.641	567.8239			1116.63	558.8186	P	1961	<b>981.0039</b>	1943.974	972.4906	1942.99	971.9986	17
12	<b>1233.709</b>	617.3581			<b>1215.698</b>	608.3528	V	1863.948	<b>932.4775</b>	1846.921	923.9642	1845.937	923.4722	16
13	1330.762	665.8845			1312.751	656.8792	P	1764.879	<b>882.9433</b>	1747.853	874.43	1746.869	873.938	15
14	1427.814	714.4109			1409.804	705.4056	P	1667.827	<b>834.4169</b>	1650.8	<b>825.9036</b>	1649.816	<b>825.4116</b>	14
15	1540.899	770.9529			1522.888	761.9476	L	1570.774	785.8905	1553.747	777.3772	1552.763	776.8852	13
16	1627.931	814.4689			1609.92	805.4636	S	1457.69	729.3485	1440.663	720.8352	1439.679	720.3432	12
17	1724.983	862.9953			1706.973	853.99	P	1370.658	685.8325	1353.631	677.3192	1352.647	676.8272	11
18	1838.067	919.5373			1820.057	910.532	I	1273.605	<b>637.3061</b>	1256.578	628.7928	1255.594	628.3008	10
19	1975.126	988.0668			1957.116	979.0615	H	1160.521	580.764	1143.494	572.2508	1142.51	571.7588	9
20	2062.158	1031.583			2044.148	1022.578	S	1023.462	<b>512.2346</b>	1006.435	503.7213	1005.451	503.2293	8
21	2176.201	1088.604	2159.175	1080.091	2158.191	1079.599	N	936.4299	468.7186	919.4033	460.2053	918.4193	459.7133	7
22	2304.26	1152.634	2287.233	1144.12	2286.249	1143.628	Q	822.3869	411.6971	805.3604	403.1838	804.3764	402.6918	6
23	2432.318	<b>1216.663</b>	2415.292	1208.15	2414.308	1207.658	Q	694.3284	347.6678	677.3018	339.1545	676.3178	338.6625	5
24	2613.332	1307.17	2596.306	1298.657	2595.322	1298.165	T	566.2698	283.6385	549.2432	275.1253	548.2592	274.6332	4
25	2726.417	1363.712	2709.39	1355.199	2708.406	1354.707	L	385.2558	193.1315	368.2292	184.6183			3
26	2823.469	1412.238	2806.443	1403.725	2805.459	1403.233	P	272.1717	136.5895	255.1452	128.0762			2
27							R	175.119	88.0631	158.0924	79.5498			1

Figure S1 Mascot search results



# Mascot Search Results

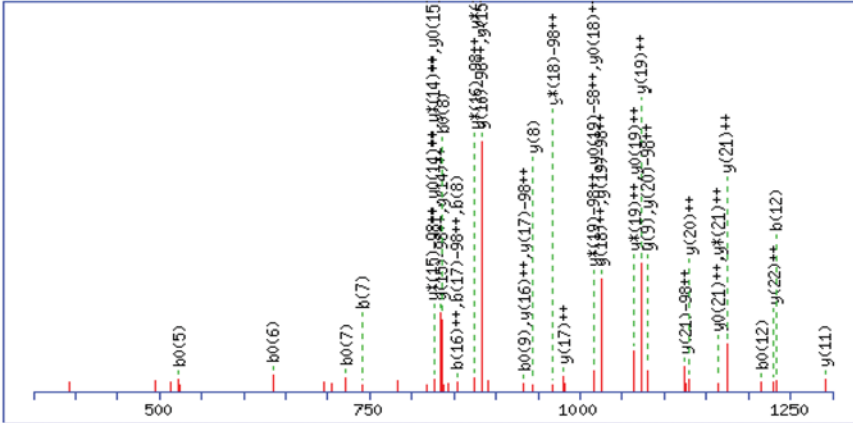
## Peptide View

MS/MS Fragmentation of **ELSPLISLPSPVPPLpSPIHSNQQTLPR**

Found in **IPI00396310**, Tax\_Id=9606 Gene\_Symbol=AFF1 AF4/FMR2 family, member 1

Match to Query 569: 2996.648172 from(999.890000,3+) intensity(4982059.0000)

Title: Cmpd 524, +MSn(1000.5), 23.8 min



The  $y_{14}^{2+}$  (834.2 m/z) and  $y_{11}$  (1290.8 m/z) ion fragments were ruled out phosphorylation at serine 212. (The amino acid positions are referred to Swiss-Prot entry [P51825](#))

Monoisotopic mass of neutral peptide Mr(calc): 2996.5736

Ions Score: 47 Expect: 0.0093

Matches (Bold Red): 46/412 fragment ions using 43 most intense peaks

#	b	b <sup>++</sup>	b <sup>*</sup>	b <sup>+++</sup>	b <sup>0</sup>	b <sup>0++</sup>	Seq.	y	y <sup>++</sup>	y <sup>*</sup>	y <sup>+++</sup>	y <sup>0</sup>	y <sup>0++</sup>	#
1	130.0499	65.5286			112.0393	56.5233	E							27
2	243.1339	122.0706			225.1234	113.0653	L	2868.538	1434.773	2851.512	1426.26	2850.528	1425.768	26
3	330.166	165.5866			312.1554	156.5813	S	2755.454	1378.231	2738.428	1369.718	2737.444	1369.226	25
4	427.2187	214.113			409.2082	205.1077	P	2668.422	1334.715	2651.396	1326.202	2650.412	1325.71	24
5	540.3028	270.655			<b>522.2922</b>	261.6498	L	2571.369	1286.188	2554.343	1277.675	2553.359	1277.183	23
6	653.3869	327.1971			<b>635.3763</b>	318.1918	I	2458.285	<b>1229.646</b>	2441.259	1221.133	2440.275	1220.641	22
7	<b>740.4189</b>	370.7131			<b>722.4083</b>	361.7078	S	2345.201	<b>1173.104</b>	2328.175	<b>1164.591</b>	2327.191	<b>1164.099</b>	21
8	<b>853.5029</b>	427.2551			<b>835.4924</b>	418.2498	L	2258.169	<b>1129.588</b>	2241.143	1121.075	2240.159	1120.583	20
9	950.5557	475.7815			<b>932.5451</b>	466.7762	P	2145.085	<b>1073.046</b>	2128.059	<b>1064.533</b>	2127.075	<b>1064.041</b>	19
10	1037.588	519.2975			1019.577	510.2922	S	2048.033	<b>1024.52</b>	2031.006	<b>1016.007</b>	2030.022	<b>1015.515</b>	18
11	1134.641	567.8239			1116.63	558.8186	P	1961	<b>981.0039</b>	1943.974	972.4906	1942.99	971.9986	17
12	<b>1233.709</b>	617.3581			<b>1215.698</b>	608.3528	V	1863.948	<b>932.4775</b>	1846.921	923.9642	1845.937	923.4722	16
13	1330.762	665.8845			1312.751	656.8792	P	1764.879	<b>882.9433</b>	1747.853	<b>874.43</b>	1746.869	<b>873.938</b>	15
14	1427.814	714.4109			1409.804	705.4056	P	1667.827	<b>834.4169</b>	1650.8	<b>825.9036</b>	1649.816	<b>825.4116</b>	14
15	1540.899	770.9529			1522.888	761.9476	L	1570.774	785.8905	1553.747	777.3772	1552.763	776.8852	13
16	1707.897	<b>854.4521</b>			1689.886	845.4468	S	1457.69	729.3485	1440.663	720.8352	1439.679	720.3432	12
17	1804.95	902.9784			1786.939	893.9732	P	<b>1290.691</b>	645.8493	1273.665	637.336	1272.681	636.844	11
18	1918.034	959.5205			1900.023	950.5152	I	1193.639	597.3229	1176.612	588.8096	1175.628	588.3176	10
19	2055.093	1028.05			2037.082	1019.045	H	<b>1080.555</b>	540.7809	1063.528	532.2676	1062.544	531.7756	9
20	2142.125	1071.566			2124.114	1062.561	S	<b>943.4956</b>	472.2514	926.469	463.7381	925.485	463.2461	8
21	2256.168	1128.587	2239.141	1120.074	2238.157	1119.582	N	856.4635	428.7354	839.437	420.2221	838.453	419.7301	7
22	2384.226	1192.617	2367.2	1184.103	2366.216	1183.611	Q	742.4206	371.7139	725.3941	363.2007	724.4101	362.7087	6
23	2512.285	1256.646	2495.258	1248.133	2494.274	1247.641	Q	614.362	307.6847	597.3355	299.1714	596.3515	298.6794	5
24	2613.332	1307.17	2596.306	1298.657	2595.322	1298.165	T	486.3035	243.6554	469.2769	235.1421	468.2929	234.6501	4
25	2726.417	1363.712	2709.39	1355.199	2708.406	1354.707	L	385.2558	193.1315	368.2292	184.6183			3
26	2823.469	1412.238	2806.443	1403.725	2805.459	1403.233	P	272.1717	136.5895	255.1452	128.0762			2
27							R	175.119	88.0631	158.0924	79.5498			1

Figure S1 Continued



# Mascot Search Results

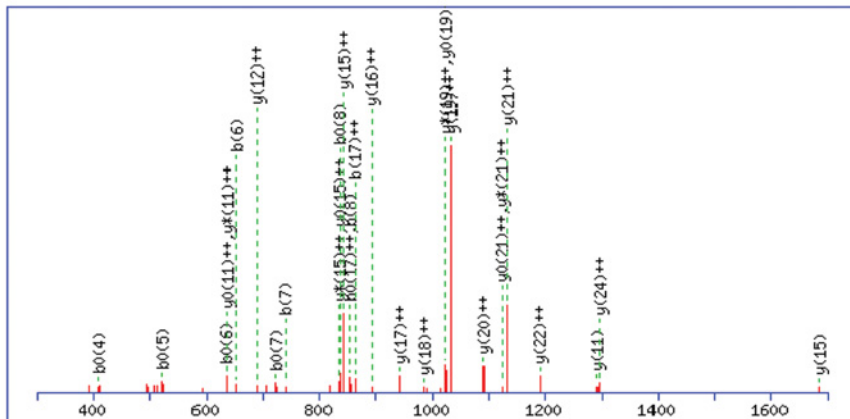
## Peptide View

MS/MS Fragmentation of **ELSPLISLSPVPPLSPIHSNQQLPR**

Found in **IPI00396310**, Tax\_Id=9606 Gene\_Symbol=AFF1 AF4/FMR2 family, member 1

Match to Query 574: 2916.758172 from(973.260000,3+) intensity(1800511.0000)

Title: Cmpd 533, +MSn(973.8), 24.1 min



Monoisotopic mass of neutral peptide Mr(calc): 2916.6073

Fixed modifications: Carbamidomethyl (C)

Ions Score: 51 Expect: 0.0037

Matches (Bold Red): 30/266 fragment ions using 38 most intense peaks

#	b	b <sup>++</sup>	b <sup>*</sup>	b <sup>**</sup>	b <sup>0</sup>	b <sup>0++</sup>	Seq.	y	y <sup>++</sup>	y <sup>*</sup>	y <sup>**</sup>	y <sup>0</sup>	y <sup>0++</sup>	#
1	130.0499	65.5286			112.0393	56.5233	E							27
2	243.1339	122.0706			225.1234	113.0653	L	2788.572	1394.79	2771.545	1386.276	2770.561	1385.784	26
3	330.166	165.5866			312.1554	156.5813	S	2675.488	1338.248	2658.461	1329.734	2657.477	1329.242	25
4	427.2187	214.113			<b>409.2082</b>	205.1077	P	2588.456	<b>1294.732</b>	2571.429	1286.218	2570.445	1285.726	24
5	540.3028	270.655			<b>522.2922</b>	261.6498	L	2491.403	1246.205	2474.377	1237.692	2473.393	1237.2	23
6	<b>653.3869</b>	327.1971			<b>635.3763</b>	318.1918	I	2378.319	<b>1189.663</b>	2361.293	1181.15	2360.309	1180.658	22
7	<b>740.4189</b>	370.7131			<b>722.4083</b>	361.7078	S	2265.235	<b>1133.121</b>	2248.208	<b>1124.608</b>	2247.224	<b>1124.116</b>	21
8	<b>853.5029</b>	427.2551			<b>835.4924</b>	418.2498	L	2178.203	<b>1089.605</b>	2161.176	1081.092	2160.192	1080.6	20
9	950.5557	475.7815			932.5451	466.7762	P	2065.119	<b>1033.063</b>	2048.092	<b>1024.55</b>	2047.108	<b>1024.058</b>	19
10	1037.588	519.2975			1019.577	510.2922	S	1968.066	<b>984.5367</b>	1951.04	976.0234	1950.056	975.5314	18
11	1134.641	567.8239			1116.63	558.8186	P	1881.034	<b>941.0207</b>	1864.008	932.5074	1863.024	932.0154	17
12	1233.709	617.3581			1215.698	608.3528	V	1783.981	<b>892.4943</b>	1766.955	883.981	1765.971	883.489	16
13	1330.762	665.8845			1312.751	656.8792	P	<b>1684.913</b>	<b>842.9601</b>	1667.886	<b>834.4468</b>	1666.902	<b>833.9548</b>	15
14	1427.814	714.4109			1409.804	705.4056	P	1587.86	794.4337	1570.834	785.9204	1569.85	785.4284	14
15	1540.899	770.9529			1522.888	761.9476	L	1490.807	745.9073	1473.781	737.3941	1472.797	736.9021	13
16	1627.931	814.4689			1609.92	805.4636	S	1377.723	<b>689.3653</b>	1360.697	680.852	1359.713	680.36	12
17	1724.983	<b>862.9953</b>			1706.973	<b>853.99</b>	P	<b>1290.691</b>	645.8493	1273.665	<b>637.336</b>	1272.681	<b>636.844</b>	11
18	1838.067	919.5373			1820.057	910.532	I	1193.639	597.3229	1176.612	588.8096	1175.628	588.3176	10
19	1975.126	988.0668			1957.116	979.0615	H	1080.555	540.7809	1063.528	532.2676	1062.544	531.7756	9
20	2062.158	1031.583			2044.148	1022.578	S	943.4956	472.2514	926.469	463.7381	925.485	463.2461	8
21	2176.201	1088.604	2159.175	1080.091	2158.191	1079.599	N	856.4635	428.7354	839.437	420.2221	838.453	419.7301	7
22	2304.26	1152.634	2287.233	1144.12	2286.249	1143.628	Q	742.4206	371.7139	725.3941	363.2007	724.4101	362.7087	6
23	2432.318	1216.663	2415.292	1208.15	2414.308	1207.658	Q	614.362	307.6847	597.3355	299.1714	596.3515	298.6794	5
24	2533.366	1267.187	2516.34	1258.673	2515.356	1258.181	T	486.3035	243.6554	469.2769	235.1421	468.2929	234.6501	4
25	2646.45	1323.729	2629.424	1315.215	2628.44	1314.723	L	385.2558	193.1315	368.2292	184.6183			3
26	2743.503	1372.255	2726.476	1363.742	2725.492	1363.25	P	272.1717	136.5895	255.1452	128.0762			2
27							R	175.119	88.0631	158.0924	79.5498			1

Figure S1 Continued

**Table S1 Identification of AF4-1-interacting proteins by nano-LC-ESI-MS/MS**

Gene symbol	Identified peptide sequence	Precursor mass ( <i>m/z</i> )	Charge state ( <i>z</i> )	Mass errors (p.p.m.)	Single peptide Mascot score	Sequence coverage
Transcription regulatory protein						
<i>PPARBP</i>	SLGMNASVTIEGTSVAVK	922.54	2+	16	77	3%
	GNNQADTVDFSIISVAGK	918.55	2+	16	71	
<i>MED12</i>	IEGTLGVLYDQPR	730.89	2+	0	67	2%
	LNLVGGMFDTVQR	733.41	2+	47	68	
<i>CRSP2</i>	FLGSVIMR	469.87	2+	23	41	8%
	AGTSSQTMPTNMPPPR	852.90	2+	11	41	
	SLLDCTFR	506.44	2+	37	45	
	ENIQDLVFR	567.50	2+	35	49	
	DGAYSFLDNSK	608.86	2+	31	43	
	LELFPDQATQK	701.91	2+	42	47	
	QGECTIFA AVR	626.36	2+	39	47	
	LVEGFYPAPGLK	645.95	2+	39	48	
	LEILVEDKETGDGR	671.45	3+	27	61	
	TFLNMFVDSNQDAR	837.45	2+	17	94	
<i>CRSP3</i>	EVGNALLNVVLK	635.07	2+	18	47	9%
	NALADFLPVMK	617.91	2+	12	43	
	FLELLPVSK	523.41	2+	17	43	
	LITALGSSEVQPQFTR	874.03	2+	13	46	
	LFDLLYPEK	569.48	2+	29	54	
	NACLLPAYFAVTEIR	869.48	2+	28	54	
	SSVALPALVETYSR	782.50	2+	10	55	
	EVGNALLNVVLK	635.07	2+	29	61	
	TVLSAESEELNR	674.33	2+	14	71	
<i>THRAP4</i>	QLAGPLFSENTLQFYNER	1064.10	2+	15	43	4%
	GSVLQFMPFTVSELVK	950.20	2+	10	40	
<i>CRSP6</i>	AAATIDSLASR	538.30	2+	37	57	6%
	VLITSQGYEQICK	769.95	2+	35	76	
<i>CRSP7</i>	LLQAIDPQSNIR	684.38	2+	14	45	6%
	AGLSPAPELLSR	605.89	2+	7	54	
	NEIIQSYLSR	611.82	2+	8	51	
<i>RBBP4</i>	TPSSDVLVFDYTK	736.38	2+	27	104	4%
<i>RUVBL2</i>	GLGLDDALEPR	578.75	2+	80	50	3%
<i>EAF1</i>	GDEVTTILPHIGSTPPMTVFK	785.06	3+	17	70	9%
<i>MED4</i>	LLSALEDLEVLRSR	729.44	2+	20	73	17%
	EAEQILATAVYQAK	767.75	2+	26	76	
	LGGGLGVAGGNSTR	608.33	2+	26	62	
<i>CRSP8</i>	GYNENVYTEDGK	694.85	2+	12	64	33%
	AFIAHFQDNLHNSVNR	590.37	2+	18	51	
	AQPTTLVLPQYVDDVISR	704.66	3+	8	48	
	SNYQVFQK	507.26	2+	9	47	
<i>MED7</i>	EYTDENIQEGLAPKPPPIK	514.33	3+	58	44	9%
<i>MED6</i>	VDALLDLR	514.39	2+	15	47	17%
	QRVDALLDLR	647.92	2+	7	47	
	VLTAVHGIQSAFDEAMSYCR	757.73	3+	12	48	
<i>MED8</i>	NQVIPLVLSADR	732.46	2+	34	65	23%
	VPVFSHEVVPDHLR	544.35	3+	10	40	
	QTFNPTDTNALVA AVFGK	983.07	2+	16	115	
	NQVIPLVLSADRDELMR	741.72	3+	13	44	
<i>TRFP</i>	SVQQTVELLTR	637.38	2+	31	53	10%
	YQYCDFLVK	618.20	2+	16	56	
<i>MED21</i>	IQSALADIAQSQLK	743.44	2+	40	55	10%
<i>ELL</i>	TSLLLLR	405.29	2+	22	49	5%
	EPVQALPSSASR	924.12	2+	0	41	
<i>PCQAP</i>	TFVPAMTAIHGPPITAPVCTR	784.68	2+	18	46	12%
	QSIPSVLQGEVAR	692.45	2+	14	58	
	SLLDILTDPK	601.51	3+	19	61	
<i>TCEA1</i>	NIPMTLELLQSTR	766.43	2+	39	63	5%
DNA-directed RNA polymerase						
<i>POLR2A</i>	TVITPDPNLSIDQGVVPR	961.01	2+	16	61	1%
<i>POLR2B</i>	AGVSQVLNR	472.27	2+	0	45	4%
	NLTYSAPLYVDITK	799.43	2+	6	47	
	TVTLPENEDELESTNR	923.89	2+	18	60	
<i>POLR2C</i>	ITELTDENVK	581.27	2+	10	55	12%
	LGLIPLISDDIVDK	755.92	2+	12	42	
	FIIENTDLAVANSIR	838.42	2+	16	82	



Table S1 Continued

Gene symbol	Identified peptide sequence	Precursor mass ( <i>m/z</i> )	Charge state ( <i>z</i> )	Mass errors (p.p.m.)	Single peptide Mascot score	Sequence coverage
DNA-binding protein						
<i>MCM3</i>	GSSGVGLTAAVTTDQETGER	968.44	2+	20	100	3%
<i>RUVBL1</i>	TALALAIQELGSK	693.38	2+	14	70	3%
RNA-binding protein						
<i>NCL</i>	SISLYYTGEK	580.96	2+	28	47	8%
	GFGFVDFNSEEDAK	781.40	2+	17	50	
	NDLAVVDVR	500.84	2+	13	55	
	GLSEDTTEETLKESFDGSVR	734.06	3+	13	62	
<i>PRPF31</i>	IYEVESR	529.66	2+	18	47	14%
	LGLTEIR	401.20	2+	11	47	
	IMGVAGGLTNLSK	638.87	2+	39	64	
	MPACNIMLLGAQR	754.01	2+	19	40	
	SSGTASSVAFTPLQGLEIVNPQAAEK	868.14	3+	27	41	
<i>SNRPD2</i>	GDSVIVVLR	479.27	2+	16	47	17%
Protein serine/threonine kinase protein						
<i>CDK9</i>	LADFLGAR	431.75	2+	11	42	43%
	LLVLDPAQR	512.84	2+	18	42	
	DPYALDLIDK	581.80	2+	8	54	
	IGQGTGGEVFK	591.81	2+	0	63	
	NPATTNQTEFER	704.33	2+	0	65	
	HENVVNLIEICR	784.45	2+	8	72	
	AYVRDPYALDLIDK	551.32	2+	18	45	
	NPATTNQTEFERVF	827.70	2+	16	59	
	QYDSVECPFCDEVSK	931.84	2+	13	63	
	VLMENEKEGFPIALR	621.67	3+	16	42	
	VVTLWYRPELLEGER	647.93	3+	15	45	
Serine/threonine phosphatase protein						
<i>PPP2R1A</i>	IGPILDNSTLQSEVKPILEK	732.21	3+	26	55	6%
	VLAMSGDPNYLHR	496.78	3+	17	47	
Translation regulator protein						
<i>EEF1B2</i>	SPAGLQVLNDYLADK	802.45	2+	43	88	7%
Auxiliary transport protein						
<i>GDI2</i>	LYSESLAR	469.70	2+	16	42	4%
	FVSISDLLVPK	609.30	2+	18	48	
	TDDYLDQPCYETINR	952.30	2+	14	49	
Receptor signalling complex scaffold protein						
<i>YWHAE</i>	EAAENSLVAYK	597.84	2+	12	41	29%
	DSTLIMQLLR	603.33	2+	0	51	
	EALQDVEDENQ	645.21	2+	10	56	
	VAGMDVELTVEER	732.36	2+	6	97	
	LICCDILDVLDK	738.93	2+	14	74	
	AASDIAMTELPPTHPIR	612.70	2+	15	76	
<i>YWHAQ</i>	DSTLIMQLLR	595.32	2+	13	49	38%
	YLAEVACGDDR	634.73	2+	18	59	
	YLIANATNPESK	660.83	2+	13	65	
	SICTTVLELLDK/AVTEQGAELSNEER	696.45	2+	10	73	
	QTIDNSQGAYQEAFFDISK	766.99	2+	16	97	
	QTIDNSQGAYQEAFFDISK	999.51	2+	10	81	
<i>SPIN</i>	VSALEVLVLPDR	549.81	2+	18	57	4%
<i>AP3S1</i>	SEAGLAGAPAR	500.27	2+	39	55	6%
Signal transduction						
<i>CCNT1</i>	QLENMEANVK	587.87	2+	17	48	38%
	QQAANLLQDMGQR	736.55	2+	27	71	
	TYSLSSSFSSSSSTR	792.37	2+	12	88	
	GPSEETGGAVFDHPAK	800.02	2+	11	78	
	MPIEGSENPERPFLEK	940.48	2+	26	40	
	SQYAYAAQNLLSHHDSHSSVILK	857.12	2+	27	73	
	SGNTDKPRPPPLPSEPPPLPPLPK	876.24	3+	18	50	
	TSENALTGVDHSLPQDGSNAFISQK	910.82	3+	16	60	
<i>S100A8</i>	LLETECPQYIR	711.37	2+	14	53	25%
<i>S100A9</i>	NIETIINTFHQYSVK	904.09	2+	12	54	21%
	KDLQNFLK	503.28	2+	19	42	
Transmembrane receptor protein tyrosine kinase protein						
<i>FGFR2</i>	NVLVTENVMKIADFGLAR	702.03	3+	19	40	3%
Lipid kinase protein						

Table S1 Continued

Gene symbol	Identified peptide sequence	Precursor mass ( <i>m/z</i> )	Charge state ( <i>z</i> )	Mass errors (p.p.m.)	Single peptide Mascot score	Sequence coverage
<i>PIP5K2B</i>	FGIDDDQYQNSVTR	829.33	2+	14	88	8%
	FFGPGGFDPSSVDVYAMK	961.47	2+	16	42	
<i>PIP5K2C</i>	FGIDDDQDYLVSLTR	821.49	2+	17	96	11%
	VSVDNEDSYMVLVLR	837.40	2+	24	94	
	DRFGIDDDQDYLVSLTR	638.40	3+	13	57	
Heterotrimeric G-protein GTPase protein						
<i>GNB4</i>	LIWDSYTTNK	677.32	2+	44	43	7%
Guanyl-nucleotide-exchange factor protein						
<i>ARHGEF4</i>	YPLQLAELLK	594.31	2+	15	41	2%
Enzyme: dehydrogenase						
<i>GAPDH</i>	VPTANVSVVDLTCR	765.90	2+	0	68	13%
	LISWYDNEFGYSNR	882.35	2+	10	64	
Enzyme: synthase						
<i>PTS</i>	VYETDNIVVYKGE	821.83	2+	73	47	10%
Unknown						
<i>SMAD9</i>	VETPVLPPVLVPR	708.45	2+	21	52	6%
	FCLGLLSNVNR	646.84	2+	7	56	
<i>LSM14A</i>	EFADFEYR	538.75	2+	18	49	12%
	SFFDNISCDDNR	745.35	2+	6	71	
	DFDFESANAQFNK	766.86	2+	32	70	
	YEGILYTIIDTENSTVALAK	1051.06	2+	19	83	
<i>DRG1</i>	IQLLDLPGIIEGAK	740.41	2+	27	41	4%
<i>HCCA2</i>	LVTDEDVFPTK	632.34	2+	14	55	10%
	EFPSFESLVR	649.36	2+	23	59	
<i>C20orf11</i>	LIMNYLVTEGFK	714.36	2+	17	13	6%

**Table S2 Analysis of control lane by nano-LC-ESI-MS/MS**

Gene symbol	Identified Peptide sequence	Precursor mass ( <i>m/z</i> )	Charge state ( <i>z</i> )	Mass errors (p.p.m.)	Single peptide Mascot score	Sequence coverage
<i>FLNA</i>	VANPSGNLTETYVQDR	767,51	2+ 2+ 2+	0	74	4%
	GAGTGGGLGAVEGPSEAK	785,93	2+	31	42	
	ANLPQSFQVDTSK	882,43	2+	62	41	
<i>JAK1</i>	LSDPGIPITVLSR	684,39	2+	14	41	3%
	SDVLTTPWKFK	661,34	2+	15	48	
<i>KIF11</i>	LTDNGTEFSVK	605,83	2+	59	47	9%
	TTAATLMNAYSSR	701,88	2+	64	55	
	ETTIDGEEELVK	617,32	2+	16	47	
	EEYITSALESTEEK	814,92	2+	48	94	
	FCALEEK	448,73	2+	33	48	
	CENIQKPLSSVQENIQK	715,02	3+	18	60	
<i>PRMT5</i>	SKVEETTEHLVTK	500,96	3+	53	64	10%
	SDLLLSGR	430,76	2+	33	49	
	KGFPVLSK	438,30	2+	68	42	
	YSQYQQAIIYK	646,33	2+	15	74	
	DTNVQVLMVLGAGR	744,94	2+	60	77	
	GPLVNASLR	463,81	2+	10	40	
<i>HSPA1A</i>	DPEAQFEMPYVVR	798,80	2+	37	62	9%
	NQVALNPQNTVFDAGR	605,63	3+	44	40	
	ATAGDTHLGGEDFDNR	838,37	2+	0	56	
	ARFEELCSDLFR	771,89	2+	25	57	
<i>PPM1B</i>	GGSGSGPTIEEVD	602,77	2+	0	48	8%
	YGLSSMQGWR	600,77	2+	8	50	
<i>STK38</i>	HIYFINGGDSR	691,34	2+	28	55	11%
	DNMSIVLVCFSNAPK	855,96	2+	52	80	
	LGLEDFESLK	575,56	2+	78	58	
	DIKPDNLLDSK	457,60	3+	22	53	
<i>PFKFB3</i>	LSDFGLECTGLK	605,79	2+	33	53	6%
	IGAPGVVEIK	506,74	2+	88	65	
	RFEGLTAR	475,22	2+	94	42	
	STIQTAELR	545,17	2+	73	37	
<i>TUBB</i>	YPTGESYQDLVQR	778,04	2+	43	61	12%
	VFNVGEYR	492,24	2+	20	44	
	ISVYYNEATGGK	651,2	2+	84	59	
	AILVDLEPGTMDSVR	816,37	2+	64	55	
<i>TUBB2C</i>	IMNTFSVVPSPK	668,28	2+	104	78	8%
	LAVNMVPPFR	580,27	2+	86	51	
	AVLVDLEPGTMDSVR	809,37	2+	49	41	
	FPGQLNADLR	565,75	2+	53	44	
<i>HNRPH1</i>	LAVNMVPPFR	580,27	2+	86	51	12%
	GLPWSCSADEVQR	752,78	2+	86	63	
	SNNVEMDWVLK	675,78	2+	59	58	
	YDGGSTFQSTTGHCVMHR	705,24	3+	85	41	
<i>PFKFB3</i>	VHIEIGPDGR	546,80	2+	9	42	8%
	EGGQIAVFDATNTR	790,29	2+	126	58	
	YPTGESYQDLVQR	778,26	2+	140	109	
<i>TUBA1A</i>	LEPVIMELER	622,74	2+	144	41	5%
	EIIDLVDR	543,29	2+	46	41	
<i>ATP5A1</i>	DVNAAIATIK	508,23	2+	128	58	4%
	VVDALGNAIDGK	586,28	2+	68	52	
<i>TRIM21</i>	AVDSLPIGR	513,79	2+	19	40	4%
	NFLVEEEQR	582,33	2+	68	37	
<i>MYC</i>	DLDITSPELR	579,79	2+	25	62	5%
	STTTGHLIYK	560,77	2+	62	40	
<i>ACTB</i>	IGGIGTVPVGR	513,30	2+	19	64	16%
	AVFPSIVGRPR	559,91	2+	91	49	
	DSYVGDEAQSQR	977,51	2+	22	61	
	GYSFTTTAER	566,77	2+	8	50	
<i>WDR77</i>	SYELPDGQVITIGNER	895,93	2+	22	52	8%
	EITALAPSTMK	589,27	2+	67	44	
	ETPPPLPPAAR	622,8	2+	88	87	
	SDGALLLGASSLSGR	702,37	2+	14	87	

**Table S3** *In silico* analysis of AF4 interactors by HPRD (<http://www.hprd.org>)

Gene name	Interactors	Type of interaction
Transcription regulatory protein <i>PPARBP</i>	14-3-3 Eta (*)	Direct
	Androgen receptor	Direct
	CRSP2 (*)	Direct
	Estrogen receptor alpha	Direct
	Estrogen receptor beta	Direct
	GATA binding protein 1	Direct
	GATA binding protein 3	Direct
	Hepatocyte nuclear factor 4 alpha	Direct
	Nuclear receptor subfamily 4, group A, member 1	Direct
	Peroxisome proliferator activated receptor gamma	Direct
	Peroxisome proliferator activated receptor, alpha	Direct
	RAR related orphan receptor A	Direct
	Retinoid X receptor, alpha	Direct
	TRAP230 (*)	Direct
	Vitamin D receptor	Direct
	p53	Direct
	NR113	Direct
	TRAP220 (*)	Direct
	PPAR gamma coactivator 1	Direct
	Retinoic acid receptor alpha	Direct
	Mediator of RNA polymerase II transcription subunit 8 (*)	Direct
	Thyroid hormone receptor alpha	Direct
	Thyroid hormone receptor, beta	Direct
	GATA binding protein 4	Direct
	GATA binding protein 6	Direct
	Mediator of RNA polymerase II transcription subunit 25 homologue	Direct
	MED9	Direct
	Surfeit 5	Complex
	TRAP230 (*)	
	CRSP2 (*)	
	Transcriptional coactivator CRSP130 (*)	
	Positive cofactor 2 glutamine	
	TRAP100 (*)	
	Transcriptional coactivator CRSP70 (*)	
	Cyclin dependent kinase 8	
	Cell division cycle 2 like 1	
	Vitamin D receptor interacting protein (*)	
	Mediator of RNA polymerase II transcription subunit 19	
	RNA polymerase II transcriptional regulation mediator (*)	
	Mediator of RNA polymerase II transcription subunit 8 (*)	
	MED18	
	Trf proximal protein	
	MED9	
	TRAP95	
	Mediator complex subunit 28	
	THRAP2	
	Thyroid hormone receptor associated protein 1	
	Mediator of RNA polymerase II transcription subunit 25 homologue	
	TRAP 80 (*)	
	CRSP9 (*)	
	MED9	
	Intersex like	
	Thyroid hormone receptor associated protein 6	
	Mediator complex subunit 28	
	Similar to HSPC296	
	Mediator of RNA polymerase II transcription, subunit 31 homologue	
SRB7		
Thyroid hormone receptor associated protein 1	Complex	
TRAP230 (*)		
CRSP2 (*)		
Transcriptional coactivator CRSP130 (*)		
Positive cofactor 2 glutamine		
TRAP100 (*)		
Mediator of RNA polymerase II transcription subunit 25 homologue		
TRAP 80 (*)		
Vitamin D receptor interacting protein (*)		
RNA polymerase II transcriptional regulation mediator (*)		
Mediator of RNA polymerase II transcription subunit 8 (*)		

**Table S3 Continued**

Gene name	Interactors	Type of interaction
	Trf proximal protein	
	Thyroid hormone receptor associated protein 6	
	SRB7	
	CRSP9 (*)	
	Mediator complex subunit 28	
	Cyclin C	Complex
	CRSP2 (*)	
	RNA polymerase II transcriptional regulation mediator (*)	
	Cyclin dependent kinase 8	
	TRAP100 (*)	
	SRB7	
	Cyclin C	Complex
	Cyclin dependent kinase 8	
	Vitamin D receptor interacting protein (*)	
	RNA polymerase II transcriptional regulation mediator (*)	
	Trf proximal protein	
	Mediator of RNA polymerase II transcription, subunit 31 homologue	
	TRAP 80 (*)	
	Mediator complex subunit 28	
	Thyroid hormone receptor associated protein 1	
	TRAP230 (*)	
	CRSP2 (*)	
	Transcriptional coactivator CRSP130 (*)	
	Thyroid hormone receptor associated protein 6	
	SRB7	
	TRAP100 (*)	
	TRAP95	
	CRSP9 (*)	
	Mediator complex subunit 28	Complex
	Thyroid hormone receptor associated protein 1	
	TRAP230 (*)	
	CRSP2 (*)	
	Transcriptional coactivator CRSP130 (*)	
	TRAP100 (*)	
	TRAP95	
	Mediator of RNA polymerase II transcription subunit 25 homologue	
	TRAP 80 (*)	
	Transcriptional coactivator CRSP70 (*)	
	Vitamin D receptor interacting protein (*)	
	RNA polymerase II transcriptional regulation mediator (*)	
	SRB7	
	CRSP9 (*)	
	Mediator complex subunit 28	
	Surfeit 5	
	Similar to HSPC296	
	MED9	
	CRSP9 (*)	
	Mediator complex subunit 28	
	TRAP230 (*)	
	TRAP 80 (*)	
	Cyclin C	
	Cyclin dependent kinase 8	
	Mediator of RNA polymerase II transcription subunit 19	
	RNA polymerase II transcriptional regulation mediator (*)	
	Mediator of RNA polymerase II transcription subunit 8 (*)	
	MED18	
	Trf proximal protein	
	MED9	
	Intersex like	
	Thyroid hormone receptor associated protein 6	
	RING3	Complex
	Cyclin dependent kinase 8	
	RNA polymerase IIA 220 kd subunit	
	CRSP2 (*)	Complex
	Thyroid hormone receptor associated protein 1	
	TRAP230 (*)	
	Transcriptional coactivator CRSP130 (*)	
	Positive cofactor 2 glutamine	
	Mediator of RNA polymerase II transcription subunit 25 homologue	

Table S3 Continued

Gene name	Interactors	Type of interaction	
MED12	Acyl-coenzyme A dehydrogenase 8	Complex	
	Actin related protein 2/3 complex subunit 2, 34kDa		
	RNA polymerase II transcriptional regulation mediator (*)		
	Mediator of RNA polymerase II transcription subunit 8 (*)		
	Peroxisome proliferator activated receptor, alpha		
	CREBBP		
	ATP binding cassette, subfamily C, member 9		
	SRC1		
	E1A binding protein p300		
	Tryptophan rich basic protein		
	PPAR gamma coactivator 1		
	Nuclear receptor coactivator 6		
	TRAP100 (*)	Complex	
	Nuclear receptor coactivator 6 interacting protein		
	TRAP100 (*)		
	Mediator of RNA polymerase II transcription subunit 25 homologue		
	TRAP 80 (*)		
	Transcriptional coactivator CRSP70 (*)		
	RNA polymerase II transcriptional regulation mediator (*)		
	SRB7		
	SRB7		
	CRSP2 (*)		
	Transcriptional coactivator CRSP130 (*)		
	Positive cofactor 2 glutamine		Complex
	Mediator of RNA polymerase II transcription subunit 25 homologue		
	Cyclin dependent kinase 8		
	RNA polymerase II transcriptional regulation mediator (*)		
	CRSP4	Complex	
	CRSP5		
	CRSP2 (*)		
	TRAP 80 (*)		
	Transcriptional coactivator CRSP130 (*)		
	Transcriptional coactivator CRSP70 (*)		
	Transcriptional coactivator CRSP34 (*)		
	CRSP9 (*)		
	TRAP230 (*)		
	Cyclin dependent kinase 8		
	TRAP220 (*)		Direct
	Transcriptional coactivator CRSP70 (*)		
	Lysosomal trafficking regulator		
	SOX9		
	Mediator of RNA polymerase II transcription subunit 8 (*)		
Thyroid hormone receptor associated protein 1			
MED9			
Surfeit 5			
TRAP220 (*)			
CRSP2 (*)			
Transcriptional coactivator CRSP130 (*)			
Positive cofactor 2 glutamine	Complex		
TRAP100 (*)			
Transcriptional coactivator CRSP70 (*)			
Cyclin dependent kinase 8			
Cell division cycle 2 like 1			
Vitamin D receptor interacting protein (*)			
Mediator of RNA polymerase II transcription subunit 19			
RNA polymerase II transcriptional regulation mediator (*)			
Mediator of RNA polymerase II transcription subunit 8 (*)			
MED18			
Trf proximal protein			
MED9			
TRAP95			
Mediator complex subunit 28			
THRAP2			
Thyroid hormone receptor associated protein 1			
Mediator of RNA polymerase II transcription subunit 25 homologue			
TRAP 80 (*)			
CRSP9 (*)			
MED9			
Intersex like			



Table S3 Continued

Gene name	Interactors	Type of interaction
CRSP2	Thyroid hormone receptor associated protein 6	Complex
	CRSP2 (*)	
	Thyroid hormone receptor associated protein 1	Complex
	TRAP220 (*)	
	Transcriptional coactivator CRSP130 (*)	Complex
	Positive cofactor 2 glutamine	
	Mediator of RNA polymerase II transcription subunit 25 homologue	Complex
	Acyl-coenzyme A dehydrogenase 8	
	Actin related protein 2/3 complex subunit 2, 34kDa	Complex
	RNA polymerase II transcriptional regulation mediator (*)	
	Mediator of RNA polymerase II transcription subunit 8 (*)	Complex
	Glucocorticoid receptor	
	Androgen receptor	Direct
	Hepatocyte nuclear factor 4 alpha	Direct
	STAT2	Direct
	TRAP220 (*)	Direct
	Intersex like	Direct
	MED9	Direct
	Surfeit 5	Complex
	TRAP230 (*)	Complex
	TRAP220 (*)	
	Transcriptional coactivator CRSP130 (*)	Complex
	Positive cofactor 2 glutamine	
	TRAP100 (*)	Complex
	Transcriptional coactivator CRSP70 (*)	
	Cyclin dependent kinase 8	Complex
	Cell division cycle 2 like 1	
	Vitamin D receptor interacting protein (*)	Complex
	Mediator of RNA polymerase II transcription subunit 19	
	RNA polymerase II transcriptional regulation mediator (*)	Complex
	Mediator of RNA polymerase II transcription subunit 8 (*)	
	MED18	Complex
	Trf proximal protein	
	MED9	Complex
	TRAP95	
	Mediator complex subunit 28	Complex
	THRAP2	
	Thyroid hormone receptor associated protein 1	Complex
	Mediator of RNA polymerase II transcription subunit 25 homologue	
	TRAP 80 (*)	Complex
	CRSP9 (*)	
	MED9	Complex
Intersex like		
Thyroid hormone receptor associated protein 6	Complex	
Mediator complex subunit 28		
Similar to HSPC296	Complex	
Mediator of RNA polymerase II transcription, subunit 31 homologue		
SRB7	Complex	
Thyroid hormone receptor associated protein 1		
TRAP230 (*)	Complex	
TRAP220 (*)		
Transcriptional coactivator CRSP130 (*)	Complex	
Positive cofactor 2 glutamine		
TRAP100 (*)	Complex	
Mediator of RNA polymerase II transcription subunit 25 homologue		
TRAP 80 (*)	Complex	
Vitamin D receptor interacting protein (*)		
RNA polymerase II transcriptional regulation mediator (*)	Complex	
Mediator of RNA polymerase II transcription subunit 8 (*)		
Trf proximal protein	Complex	
Thyroid hormone receptor associated protein 6		
SRB7	Complex	
CRSP9 (*)		
Mediator complex subunit 28	Complex	
Cyclin C		
RNA polymerase II transcriptional regulation mediator (*)	Complex	
Cyclin dependent kinase 8		
TRAP220 (*)	Complex	
TRAP100 (*)		





Table S3 Continued

Gene name	Interactors	Type of interaction	
CRSP3	SRB7	Complex	
	SRB7		
	TRAP220 (*)		
	Transcriptional coactivator CRSP130 (*)		
	Positive cofactor 2 glutamine		
	CRSP4		
	CRSP5		
	TRAP 80 (*)		
	TRAP220 (*)		
	Transcriptional coactivator CRSP130 (*)		
	Transcriptional coactivator CRSP70 (*)		
	Transcriptional coactivator CRSP34 (*)		
	CRSP9 (*)		
	CCAAT/Enhancer binding protein, beta		Direct
	E74 like factor 3		Direct
	Nuclear receptor coactivator 6		Direct
	Thyroid hormone receptor associated protein 1		Direct
	Pumilio2	Direct	
	WD and tetratricopeptide repeats 1	Direct	
	Forkhead box J3	Direct	
	MED9	Direct	
	Surfeit 5	Complex	
	TRAP230 (*)	Complex	
	TRAP220 (*)		
	CRSP2 (*)		
	Positive cofactor 2 glutamine		
	TRAP100 (*)		
	Transcriptional coactivator CRSP70 (*)		
	Cyclin dependent kinase 8		
	Cell division cycle 2 like 1		
	Vitamin D receptor interacting protein (*)		
	Mediator of RNA polymerase II transcription subunit 19		
	RNA polymerase II transcriptional regulation mediator (*)		
	Mediator of RNA polymerase II transcription subunit 8 (*)		
	MED18		
	Trf proximal protein		
	MED9		
	TRAP95		
	Mediator complex subunit 28		
	THRAP2		
	Thyroid hormone receptor associated protein 1		
	Mediator of RNA polymerase II transcription subunit 25 homologue		
	TRAP 80 (*)		
	CRSP9 (*)		
	MED9		
	Intersex like		
	Thyroid hormone receptor associated protein 6		
Mediator complex subunit 28			
Similar to HSPC296			
Mediator of RNA polymerase II transcription, subunit 31 homologue			
SRB7	Complex		
Thyroid hormone receptor associated protein 1			
TRAP230 (*)			
TRAP220 (*)			
CRSP2 (*)			
Positive cofactor 2 glutamine			
TRAP100 (*)			
Mediator of RNA polymerase II transcription subunit 25 homologue			
TRAP 80 (*)			
Vitamin D receptor interacting protein (*)			
RNA polymerase II transcriptional regulation mediator (*)			
Mediator of RNA polymerase II transcription subunit 8 (*)			
Trf proximal protein			
Thyroid hormone receptor associated protein 6			
SRB7		Complex	
CRSP9 (*)			
Mediator complex subunit 28			
Cyclin C			
	Cyclin dependent kinase 8		

**Table S3 Continued**

Gene name	Interactors	Type of interaction
	Vitamin D receptor interacting protein (*) RNA polymerase II transcriptional regulation mediator (*) Trf proximal protein Mediator of RNA polymerase II transcription, subunit 31 homologue TRAP 80 (*) Mediator complex subunit 28 Thyroid hormone receptor associated protein 1 TRAP230 (*) TRAP220 (*) CRSP2 (*) Thyroid hormone receptor associated protein 6 SRB7 TRAP100 (*) TRAP95 CRSP9 (*) Mediator complex subunit 28 Thyroid hormone receptor associated protein 1 TRAP230 (*) TRAP220 (*) CRSP2 (*) TRAP100 (*) TRAP95 Mediator of RNA polymerase II transcription subunit 25 homologue TRAP 80 (*) Transcriptional coactivator CRSP70 (*) Vitamin D receptor interacting protein (*) RNA polymerase II transcriptional regulation mediator (*) SRB7 CRSP9 (*) CRSP2 (*) Thyroid hormone receptor associated protein 1 TRAP230 (*) TRAP220 (*)	Complex
	Positive cofactor 2 glutamine Mediator of RNA polymerase II transcription subunit 25 homologue Acyl-coenzyme A dehydrogenase 8 Actin related protein 2/3 complex subunit 2, 34kDa RNA polymerase II transcriptional regulation mediator (*) Mediator of RNA polymerase II transcription subunit 8 (*) Mediator of RNA polymerase II transcription, subunit 31 homologue CRSP2 (*) Vitamin D receptor interacting protein (*) RNA polymerase II transcriptional regulation mediator (*) TRAP95 TRAP 80 (*) TRAP100 (*) Trf proximal protein Thyroid hormone receptor associated protein 6 SRB7 PC2 TRAP100 (*) Mediator of RNA polymerase II transcription subunit 25 homologue TRAP 80 (*) Transcriptional coactivator CRSP70 (*) RNA polymerase II transcriptional regulation mediator (*) SRB7 SRB7 TRAP220 (*) CRSP2 (*) Positive cofactor 2 glutamine CRSP4 CRSP5 CRSP2 (*) TRAP 80 (*) TRAP220 (*) Transcriptional coactivator CRSP70 (*) Transcriptional coactivator CRSP34 (*) CRSP9 (*)	Complex
<i>THRAP4</i>	Estrogen receptor alpha	Direct

Table S3 Continued

Gene name	Interactors	Type of interaction
	Peroxisome proliferator activated receptor gamma	Direct
	Peroxisome proliferator activated receptor, alpha	Direct
	Retinoid X receptor, alpha	Direct
	MED9	Direct
	Surfeit 5	Complex
	TRAP230 (*)	
	TRAP220 (*)	
	CRSP2 (*)	
	Transcriptional coactivator CRSP130 (*)	
	Positive cofactor 2 glutamine	
	Transcriptional coactivator CRSP70 (*)	
	Cyclin dependent kinase 8	
	Cell division cycle 2 like 1	
	Vitamin D receptor interacting protein (*)	
	Mediator of RNA polymerase II transcription subunit 19	
	RNA polymerase II transcriptional regulation mediator (*)	
	Mediator of RNA polymerase II transcription subunit 8 (*)	
	MED18	
	Trf proximal protein	
	MED9	
	TRAP95	
	Mediator complex subunit 28	
	THRAP2	
	Thyroid hormone receptor associated protein 1	
	Mediator of RNA polymerase II transcription subunit 25 homologue	
	TRAP 80 (*)	
	CRSP9 (*)	
	MED9	
	Intersex like	
	Thyroid hormone receptor associated protein 6	
	Mediator complex subunit 28	
	Similar to HSPC296	
	Mediator of RNA polymerase II transcription, subunit 31 homologue	
	SRB7	
	Thyroid hormone receptor associated protein 1	Complex
	TRAP230 (*)	
	TRAP220 (*)	
	CRSP2 (*)	
	Transcriptional coactivator CRSP130 (*)	
	Positive cofactor 2 glutamine	
	Mediator of RNA polymerase II transcription subunit 25 homologue	
	TRAP 80 (*)	
	Vitamin D receptor interacting protein (*)	
	RNA polymerase II transcriptional regulation mediator (*)	
	Mediator of RNA polymerase II transcription subunit 8 (*)	
	Trf proximal protein	
	Thyroid hormone receptor associated protein 6	
	SRB7	
	CRSP9 (*)	
	Mediator complex subunit 28	
	Cyclin C	Complex
	CRSP2 (*)	
	RNA polymerase II transcriptional regulation mediator (*)	
	Cyclin dependent kinase 8	
	TRAP220 (*)	
	SRB7	
	Cyclin C	Complex
	Cyclin dependent kinase 8	
	Vitamin D receptor interacting protein (*)	
	RNA polymerase II transcriptional regulation mediator (*)	
	Trf proximal protein	
	Mediator of RNA polymerase II transcription, subunit 31 homologue	
	TRAP 80 (*)	
	Mediator complex subunit 28	
	Thyroid hormone receptor associated protein 1	
	TRAP230 (*)	
	TRAP220 (*)	
	CRSP2 (*)	
	Transcriptional coactivator CRSP130 (*)	

**Table S3 Continued**

Gene name	Interactors	Type of interaction
<i>CRSP6</i>	Thyroid hormone receptor associated protein 6	Complex
	SRB7	
	TRAP95	
	CRSP9 (*)	
	Mediator complex subunit 28	
	Thyroid hormone receptor associated protein 1	
	TRAP230 (*)	
	TRAP220 (*)	
	CRSP2 (*)	
	Transcriptional coactivator CRSP130 (*)	
	TRAP95	
	Mediator of RNA polymerase II transcription subunit 25 homologue	
	TRAP 80 (*)	
	Transcriptional coactivator CRSP70 (*)	
	Vitamin D receptor interacting protein (*)	
	RNA polymerase II transcriptional regulation mediator (*)	
	SRB7	Complex
	CRSP9 (*)	
	Peroxisome proliferator activated receptor, alpha	
	CREBBP	
	ATP binding cassette, subfamily C, member 9	
	SRC1	
	E1A binding protein p300	
	Tryptophan rich basic protein	
	TRAP220 (*)	
	PPAR gamma coactivator 1	
	Nuclear receptor coactivator 6	
	Nuclear receptor coactivator 6 interacting protein	
	Mediator of RNA polymerase II transcription subunit 25 homologue	
	TRAP 80 (*)	
	Transcriptional coactivator CRSP70 (*)	
	RNA polymerase II transcriptional regulation mediator (*)	
	SRB7	
SRB7		
TRAP220 (*)		
CRSP2 (*)		
Transcriptional coactivator CRSP130 (*)		
Positive cofactor 2 glutamine		
Mediator of RNA polymerase II transcription, subunit 31 homologue		
CRSP2 (*)		
Vitamin D receptor interacting protein (*)		
RNA polymerase II transcriptional regulation mediator (*)		
TRAP95		
TRAP 80 (*)		
Transcriptional coactivator CRSP130 (*)	Complex	
Trf proximal protein		
Thyroid hormone receptor associated protein 6		
SRB7		
PC2		
Mediator of RNA polymerase II transcription subunit 19		
Surfeit 5		
Thyroid hormone receptor associated protein 6		
p53		
Mediator of RNA polymerase II transcription subunit 8 (*)		
Ubiquitin specific protease 49		
BRCA1		
BRCA1 associated ring domain 1		
SMARCA4		
RNA polymerase IIA 220 kd subunit		Complex
Surfeit 5		
TRAP230 (*)		
TRAP220 (*)		
CRSP2 (*)		
Transcriptional coactivator CRSP130 (*)		
Positive cofactor 2 glutamine		
TRAP100 (*)		
Transcriptional coactivator CRSP70 (*)		
Cyclin dependent kinase 8		
Cell division cycle 2 like 1		

Table S3 Continued

Gene name	Interactors	Type of interaction
	Vitamin D receptor interacting protein (*)	
	Mediator of RNA polymerase II transcription subunit 19	
	RNA polymerase II transcriptional regulation mediator (*)	
	Mediator of RNA polymerase II transcription subunit 8 (*)	
	MED18	
	Trf proximal protein	
	MED9	
	TRAP95	
	Mediator complex subunit 28	
	THRAP2	
	Thyroid hormone receptor associated protein 1	
	Mediator of RNA polymerase II transcription subunit 25 homologue	
	CRSP9 (*)	
	MED9	
	Intersex like	
	Thyroid hormone receptor associated protein 6	
	Mediator complex subunit 28	
	Similar to HSPC296	
	Mediator of RNA polymerase II transcription, subunit 31 homologue	
	SRB7	
	Thyroid hormone receptor associated protein 1	Complex
	TRAP230 (*)	
	TRAP220 (*)	
	CRSP2 (*)	
	Transcriptional coactivator CRSP130 (*)	
	Positive cofactor 2 glutamine	
	TRAP100 (*)	
	Mediator of RNA polymerase II transcription subunit 25 homologue	
	Vitamin D receptor interacting protein (*)	
	RNA polymerase II transcriptional regulation mediator (*)	
	Mediator of RNA polymerase II transcription subunit 8 (*)	
	Trf proximal protein	
	Thyroid hormone receptor associated protein 6	
	SRB7	
	CRSP9 (*)	
	Mediator complex subunit 28	
	Cyclin C	Complex
	Cyclin dependent kinase 8	
	Vitamin D receptor interacting protein (*)	
	RNA polymerase II transcriptional regulation mediator (*)	
	Trf proximal protein	
	Mediator of RNA polymerase II transcription, subunit 31 homologue	
	Mediator complex subunit 28	
	Thyroid hormone receptor associated protein 1	
	TRAP230 (*)	
	TRAP220 (*)	
	CRSP2 (*)	
	Transcriptional coactivator CRSP130 (*)	
	Thyroid hormone receptor associated protein 6	
	SRB7	
	TRAP100 (*)	
	TRAP95	
	CRSP9 (*)	
	Mediator complex subunit 28	Complex
	Thyroid hormone receptor associated protein 1	
	TRAP230 (*)	
	TRAP220 (*)	
	CRSP2 (*)	
	Transcriptional coactivator CRSP130 (*)	
	TRAP100 (*)	
	TRAP95	
	Mediator of RNA polymerase II transcription subunit 25 homologue	
	Transcriptional coactivator CRSP70 (*)	
	Vitamin D receptor interacting protein (*)	
	RNA polymerase II transcriptional regulation mediator (*)	
	SRB7	
	CRSP9 (*)	
	Mediator complex subunit 28	Complex
	Surfeit 5	

Table S3 Continued

Gene name	Interactors	Type of interaction
<i>CRSP7</i>	Similar to HSPC296	
	MED9	
	CRSP9 (*)	
	Mediator complex subunit 28	
	TRAP230 (*)	
	TRAP220 (*)	
	Cyclin C	
	Cyclin dependent kinase 8	
	Mediator of RNA polymerase II transcription subunit 19	
	RNA polymerase II transcriptional regulation mediator (*)	
	Mediator of RNA polymerase II transcription subunit 8 (*)	
	MED18	
	Trf proximal protein	
	MED9	
	Intersex like	
	Thyroid hormone receptor associated protein 6	
	Mediator of RNA polymerase II transcription subunit 8 (*)	Complex
	Intersex like	
	TRAP100 (*)	Complex
	Mediator of RNA polymerase II transcription subunit 25 homologue	
	Transcriptional coactivator CRSP70 (*)	
	RNA polymerase II transcriptional regulation mediator (*)	
	SRB7	
	SRB7	
	TRAP220 (*)	
	CRSP2 (*)	
	Transcriptional coactivator CRSP130 (*)	
	Positive cofactor 2 glutamine	
	Mediator of RNA polymerase II transcription, subunit 31 homologue	
	CRSP2 (*)	Complex
	Vitamin D receptor interacting protein (*)	
	RNA polymerase II transcriptional regulation mediator (*)	
	TRAP95	
	Transcriptional coactivator CRSP130 (*)	
	TRAP100 (*)	
	Trf proximal protein	
	Thyroid hormone receptor associated protein 6	
	SRB7	
	PC2	
	CRSP4	
	CRSP5	
CRSP2 (*)		
TRAP220 (*)		
Transcriptional coactivator CRSP130 (*)		
Transcriptional coactivator CRSP70 (*)		
Transcriptional coactivator CRSP34 (*)		
CRSP9 (*)		
Cyclin dependent kinase 8	Direct	
TRAP230 (*)	Direct	
Mediator of RNA polymerase II transcription subunit 8 (*)	Direct	
Retinol binding protein 1	Direct	
MED9	Direct	
Surfeit 5	Complex	
TRAP230 (*)		
TRAP220 (*)		
CRSP2 (*)		
Transcriptional coactivator CRSP130 (*)		
Positive cofactor 2 glutamine		
TRAP100 (*)		
Cyclin dependent kinase 8		
Cell division cycle 2 like 1		
Vitamin D receptor interacting protein (*)		
Mediator of RNA polymerase II transcription subunit 19		
RNA polymerase II transcriptional regulation mediator (*)		
Mediator of RNA polymerase II transcription subunit 8 (*)		
MED18		
Trf proximal protein		
MED9		
TRAP95		

Table S3 Continued

Gene name	Interactors	Type of interaction
RBBP4	Mediator complex subunit 28	Complex
	THRAP2	
	Thyroid hormone receptor associated protein 1	
	Mediator of RNA polymerase II transcription subunit 25 homologue	
	TRAP 80 (*)	
	CRSP9 (*)	
	MED9	
	Intersex like	
	Thyroid hormone receptor associated protein 6	
	Mediator complex subunit 28	
	Similar to HSPC296	
	Mediator of RNA polymerase II transcription, subunit 31 homologue	
	SRB7	
	Mediator complex subunit 28	
	Thyroid hormone receptor associated protein 1	
	TRAP230 (*)	
	TRAP220 (*)	
	CRSP2 (*)	
	Transcriptional coactivator CRSP130 (*)	
	TRAP100 (*)	
	TRAP95	
	Mediator of RNA polymerase II transcription subunit 25 homologue	
	TRAP 80 (*)	
	Vitamin D receptor interacting protein (*)	
	RNA polymerase II transcriptional regulation mediator (*)	
	SRB7	
	CRSP9 (*)	
	Mediator complex subunit 28	Complex
	MED9	
	Intersex like	
	Mediator of RNA polymerase II transcription subunit 19	Complex
	TRAP100 (*)	
	Mediator of RNA polymerase II transcription subunit 25 homologue	
	TRAP 80 (*)	Complex
	RNA polymerase II transcriptional regulation mediator (*)	
	SRB7	
	SRB7	
	TRAP220 (*)	
	CRSP2 (*)	
	Transcriptional coactivator CRSP130 (*)	
	Positive cofactor 2 glutamine	
	CRSP4	
CRSP5		
CRSP2		
TRAP 80 (*)		
TRAP220 (*)		
Transcriptional coactivator CRSP130 (*)		
Transcriptional coactivator CRSP34 (*)		
CRSP9 (*)		
BRCA1	Direct	
CREBBP	Direct	
Chromatin assembly factor 1 subunit B	Direct	
Histone H3 K9 methyltransferase 1	Direct	
Histone deacetylase 1	Direct	
Inhibitor of growth 1	Direct	
Retinoblastoma 1	Direct	
Retinoblastoma binding protein 7	Direct	
Transcription factor Sp1	Direct	
Transcription factor Sp3	Direct	
Sin3 associated polypeptide ,30KD	Direct	
Metastasis associated protein MTA1	Direct	
Methyl CpG binding domain protein 2	Direct	
Methyl CpG binding domain protein 3	Direct	
Histone deacetylase 2	Direct	
Breast cancer metastasis suppressor 1	Direct	
Retinol binding protein 1	Direct	
Metastasis associated protein MTA2	Direct	
Histone deacetylase 3	Direct	
SIN3A	Direct	



Table S3 Continued

Gene name	Interactors	Type of interaction
	Hypothetical protein MGC4677	Direct
	AE binding protein 2	Direct
	Breast cancer metastasis suppressor 1 like	Direct
	Histone deacetylase 4	Direct
	H2A histone family member Q	Direct
	Histone 2 H3c	Direct
	SHARP	Direct
	CD8 Antigen, alpha polypeptide	Complex
	Histone deacetylase 1	
	Eukaryotic translation initiation factor 3, subunit 10	
	Retinoblastoma binding protein 7	
	Chromodomain helicase DNA binding protein 4	
	Sin3 associated polypeptide ,30KD	
	Methyl CpG binding domain protein 2	
	Methyl CpG binding domain protein 3	
	Histone deacetylase 2	
	Metastasis associated protein MTA2	
	SIN3A	
	EZH2 protein	Complex
	Polycomb protein SUZ12	
	EED	
	AE binding protein 2	
	Histone deacetylase 1	Complex
	Retinoblastoma binding protein 7	
	Metastasis associated protein MTA1	
	Histone deacetylase 2	
	Metastasis associated protein MTA2	
	Methyl-CpG binding domain protein 3-like 1	
	Histone deacetylase 1	Complex
	Inhibitor of growth 1	
	Sin3 associated polypeptide ,30KD	
	Retinol binding protein 1	
	SIN3A	
	Histone deacetylase 1	Complex
	Retinoblastoma binding protein 7	
	Sin3 associated polypeptide, 18 kd	
	Sin3 associated polypeptide ,30KD	
	Histone deacetylase 2	
	Histone deacetylase 1	Complex
	Retinoblastoma binding protein 7	
	Methyl CpG binding domain protein 3	
	Histone deacetylase 2	
	Metastasis associated protein MTA2	
	Chromodomain helicase DNA binding protein 3	
	Metastasis associated protein MTA3	
	Polycomb protein SUZ12	Complex
	EED	
	Chromatin assembly factor 1 subunit B	Complex
	Chromatin assembly factor 1 subunit A	
	Sin3 associated polypeptide ,30KD	Complex
	SIN3A	
	Histone deacetylase 2	
	Histone deacetylase 1	
	Nuclear receptor corepressor 2	
	Histone deacetylase 3	
	Nuclear receptor corepressor 1	
	mSDS3	Complex
	Histone deacetylase 1	
	Retinoblastoma binding protein 7	
	Sin3 associated polypeptide ,30KD	
	Histone deacetylase 2	
	SIN3A	
	RBP1 like protein	
	mSin3A-associated protein 130	
	Sds3	Complex
	Set1	
	Heat shock 70 KD protein 1A	
	HSP90A	
	Host cell factor C1	

Table S3 Continued

Gene name	Interactors	Type of interaction
<i>RUVBL2</i>	Histone deacetylase 1	
	Retinoblastoma binding protein 7	
	Sin3 associated polypeptide ,30KD	
	ASH2 like	
	Histone deacetylase 2	
	Heat shock 70 kDa protein 8	
	SIN3A	
	SIN3B	
	WD repeat domain 5	
	Activating transcription factor 2	Direct
	BAF53	Direct
	Proliferating cell nuclear antigen	Direct
	RuvB like 1 (*)	Direct
	RuvB like 2 (*)	Direct
	Catenin beta	Direct
	Exosome component 10	Direct
	Bcl 3	Direct
	Histone deacetylase 1	Direct
	Histone deacetylase 4	Direct
	Mortality factor 4 like protein 1	Complex
	Sarcoma antigen NY-SAR-91	
	Inhibitor of growth family member 3	
	EPC1	
	Enhancer of polycomb homologue 2	
	HIV-1 Tat interacting protein, 60kDa	
	Actin beta	
	HIV-1 Tat interacting protein, 60kDa	
	Glioma amplified sequence 41	
	Bromodomain containing 8	
	350/400 kDa PCAF associated factor	
	Actin-like 6A	
	DMAP1	
	RuvB like 1 (*)	
	E1A binding protein p400	
	HIV-1 Tat interacting protein, 60kDa	Complex
	Actin beta	
	Mortality factor 4 like 2	
	HIV-1 Tat interacting protein, 60kDa	
	Inhibitor of growth family member 3	
	Glioma amplified sequence 41	
	Bromodomain containing 8	
350/400 kDa PCAF associated factor		
Actin-like 6A		
DMAP1		
E1A binding protein p400		
Mortality factor 4 like protein 1		
Sarcoma antigen NY-SAR-91		
EPC1		
Heat shock 70 KD protein 1A		
Ribosomal L1 domain containing 1		
C20orf20 protein		
RuvB like 1 (*)		
HIV-1 Tat interacting protein, 60kDa	Complex	
350/400 kDa PCAF associated factor		
Bromodomain containing 8		
E1A binding protein p400		
EPC1		
Enhancer of polycomb homologue 2		
HIV-1 Tat interacting protein, 60kDa		
Inhibitor of growth family member 3		
Mortality factor 4 like protein 1		
Mortality factor 4 like 2		
C20orf20 protein		
Sarcoma antigen NY-SAR-91		
DMAP1		
RuvB like 1 (*)		
Glioma amplified sequence 41		
Actin-like 6A		
TCFL1		

**Table S3 Continued**

Gene name	Interactors	Type of interaction
	RNA polymerase II subunit 5-mediating protein	Complex
	RuvB like 1 (*)	
	BCR downstream signaling 1	
	S phase kinase associated protein 2	
	NHP2 like protein 1	Complex
	Nucleolar protein NOP5	
	Fibrillarin	
	NHP2 like protein 1	
	NOP56	
	RuvB like 1 (*)	
	RNA	
<i>EAF1</i>	Elongation factor, RNA polymerase II, 2	Direct
	RNA polymerase II elongation factor ELL	Direct
<i>MED4</i>	MED9	Direct
	Surfeit 5	Complex
	TRAP230 (*)	
	TRAP220 (*)	
	CRSP2 (*)	
	Transcriptional coactivator CRSP130 (*)	
	Positive cofactor 2 glutamine	
	TRAP100 (*)	
	Transcriptional coactivator CRSP70 (*)	
	Cyclin dependent kinase 8	
	Cell division cycle 2 like 1	
	Mediator of RNA polymerase II transcription subunit 19	
	RNA polymerase II transcriptional regulation mediator (*)	
	Mediator of RNA polymerase II transcription subunit 8 (*)	
	MED18	
	Trf proximal protein	
	MED9	
	TRAP95	
	Mediator complex subunit 28	
	THRAP2	
	Thyroid hormone receptor associated protein 1	
	Mediator of RNA polymerase II transcription subunit 25 homologue	
	TRAP 80 (*)	
	CRSP9 (*)	
	MED9	
	Intersex like	
	Thyroid hormone receptor associated protein 6	
	Mediator complex subunit 28	
	Similar to HSPC296	
	Mediator of RNA polymerase II transcription, subunit 31 homologue	
	SRB7	
	Thyroid hormone receptor associated protein 1	Complex
	TRAP230 (*)	
	TRAP220 (*)	
	CRSP2 (*)	
	Transcriptional coactivator CRSP130 (*)	
	Positive cofactor 2 glutamine	
	TRAP100 (*)	
	Mediator of RNA polymerase II transcription subunit 25 homologue	
	TRAP 80 (*)	
	RNA polymerase II transcriptional regulation mediator (*)	
	Mediator of RNA polymerase II transcription subunit 8 (*)	
	Trf proximal protein	
	Thyroid hormone receptor associated protein 6	
	SRB7	
	CRSP9 (*)	
	Mediator complex subunit 28	
	Cyclin C	Complex
	Cyclin dependent kinase 8	
	RNA polymerase II transcriptional regulation mediator (*)	
	Trf proximal protein	
	Mediator of RNA polymerase II transcription, subunit 31 homologue	
	TRAP 80 (*)	
	Mediator complex subunit 28	
	Thyroid hormone receptor associated protein 1	

Table S3 Continued

Gene name	Interactors	Type of interaction
	TRAP230 (*)	
	TRAP220 (*)	
	CRSP2 (*)	
	Transcriptional coactivator CRSP130 (*)	
	Thyroid hormone receptor associated protein 6	
	SRB7	
	TRAP100 (*)	
	TRAP95	
	CRSP9 (*)	
	Mediator complex subunit 28	Complex
	Thyroid hormone receptor associated protein 1	
	TRAP230 (*)	
	TRAP220 (*)	
	CRSP2 (*)	
	Transcriptional coactivator CRSP130 (*)	
	TRAP100 (*)	
	TRAP95	
	Mediator of RNA polymerase II transcription subunit 25 homologue	
	TRAP 80 (*)	
	Transcriptional coactivator CRSP70 (*)	
	RNA polymerase II transcriptional regulation mediator (*)	
	SRB7	
	CRSP9 (*)	
	Mediator complex subunit 28	Complex
	CRSP2 (*)	
	TRAP95	
	RNA polymerase II transcriptional regulation mediator (*)	
	MED18	
	Trf proximal protein	
	SRB7	
	Mediator of RNA polymerase II transcription, subunit 31 homologue	Complex
	CRSP2 (*)	
	RNA polymerase II transcriptional regulation mediator (*)	
	TRAP95	
	TRAP 80 (*)	
	Transcriptional coactivator CRSP130 (*)	
	TRAP100 (*)	
	Trf proximal protein	
	Thyroid hormone receptor associated protein 6	
	SRB7	
	PC2	
<i>CRSP8</i>	Mediator of RNA polymerase II transcription subunit 19	Direct
	Surfeit 5	Direct
	Thyroid hormone receptor associated protein 6	Direct
	Mediator of RNA polymerase II transcription subunit 8 (*)	Direct
	MED9	Direct
	CRSP4	Complex
	CRSP5	
	CRSP2 (*)	
	TRAP 80 (*)	
	TRAP220 (*)	
	Transcriptional coactivator CRSP130 (*)	
	Transcriptional coactivator CRSP70 (*)	
	CRSP9 (*)	
<i>CRSP9</i>	Mediator of RNA polymerase II transcription subunit 8 (*)	Direct
	MED9	Direct
	Mediator complex subunit 28	Complex
	Surfeit 5	
	Similar to HSPC296	
	MED9	
	Mediator complex subunit 28	
	TRAP230 (*)	
	TRAP220 (*)	
	TRAP 80 (*)	
	Cyclin C	
	Cyclin dependent kinase 8	
	Mediator of RNA polymerase II transcription subunit 19	
	RNA polymerase II transcriptional regulation mediator (*)	
	Mediator of RNA polymerase II transcription subunit 8 (*)	

**Table S3 Continued**

Gene name	Interactors	Type of interaction
	MED18	
	Trf proximal protein	
	MED9	
	Intersex like	
	Thyroid hormone receptor associated protein 6	
	Surfeit 5	
	TRAP230 (*)	
	TRAP220 (*)	
	CRSP2 (*)	
	Transcriptional coactivator CRSP130 (*)	
	Positive cofactor 2 glutamine	
	TRAP100 (*)	
	Transcriptional coactivator CRSP70 (*)	
	Cyclin dependent kinase 8	
	Cell division cycle 2 like 1	
	Vitamin D receptor interacting protein (*)	
	Mediator of RNA polymerase II transcription subunit 19	
	RNA polymerase II transcriptional regulation mediator (*)	
	Mediator of RNA polymerase II transcription subunit 8 (*)	
	MED18	
	Trf proximal protein	
	MED9	
	TRAP95	
	Mediator complex subunit 28	
	THRAP2	
	Thyroid hormone receptor associated protein 1	
	Mediator of RNA polymerase II transcription subunit 25 homologue	
	TRAP 80 (*)	
	MED9	
	Intersex like	
	Thyroid hormone receptor associated protein 6	
	Mediator complex subunit 28	
	Similar to HSPC296	
	Mediator of RNA polymerase II transcription, subunit 31 homologue	
	SRB7	
	Thyroid hormone receptor associated protein 1	
	TRAP230 (*)	
	TRAP220 (*)	
	CRSP2 (*)	
	Transcriptional coactivator CRSP130 (*)	
	Positive cofactor 2 glutamine	
	TRAP100 (*)	
	Mediator of RNA polymerase II transcription subunit 25 homologue	
	TRAP 80 (*)	
	Vitamin D receptor interacting protein (*)	
	RNA polymerase II transcriptional regulation mediator (*)	
	Mediator of RNA polymerase II transcription subunit 8 (*)	
	Trf proximal protein	
	Thyroid hormone receptor associated protein 6	
	SRB7	
	Mediator complex subunit 28	
	Cyclin C	
	Cyclin dependent kinase 8	
	Vitamin D receptor interacting protein (*)	
	RNA polymerase II transcriptional regulation mediator (*)	
	Trf proximal protein	
	Mediator of RNA polymerase II transcription, subunit 31 homologue	
	TRAP 80 (*)	
	Mediator complex subunit 28	
	Thyroid hormone receptor associated protein 1	
	TRAP230 (*)	
	TRAP220 (*)	
	CRSP2 (*)	
	Transcriptional coactivator CRSP130 (*)	
	Thyroid hormone receptor associated protein 6	
	SRB7	
	TRAP100 (*)	
	TRAP95	
	Mediator complex subunit 28	

Table S3 Continued

Gene name	Interactors	Type of interaction
MED 6	Thyroid hormone receptor associated protein 1	
	TRAP230 (*)	
	TRAP220 (*)	
	CRSP2 (*)	
	Transcriptional coactivator CRSP130 (*)	
	TRAP100 (*)	
	TRAP95	
	Mediator of RNA polymerase II transcription subunit 25 homologue	
	TRAP 80 (*)	
	Transcriptional coactivator CRSP70 (*)	
	Vitamin D receptor interacting protein (*)	
	RNA polymerase II transcriptional regulation mediator (*)	
	SRB7	
	CRSP4	Complex
	CRSP5	
	CRSP2	
	TRAP 80 (*)	
	TRAP220 (*)	
	Transcriptional coactivator CRSP130 (*)	
	Transcriptional coactivator CRSP70 (*)	
	Transcriptional coactivator CRSP34 (*)	
	ADP ribosyl transferase	Direct
	Retinoic acid receptor alpha	Direct
	SMAD1	Direct
	SMAD2	Direct
	Mediator of RNA polymerase II transcription subunit 8 (*)	Direct
	Mediator of RNA polymerase II transcription subunit 25 homologue	Direct
	MED9	Direct
	Surfeit 5	Complex
	TRAP230 (*)	
	TRAP220 (*)	
	CRSP2 (*)	
	Transcriptional coactivator CRSP130 (*)	
	Positive cofactor 2 glutamine	
	TRAP100 (*)	
	Transcriptional coactivator CRSP70 (*)	
	Cyclin dependent kinase 8	
	Cell division cycle 2 like 1	
	Vitamin D receptor interacting protein (*)	
	Mediator of RNA polymerase II transcription subunit 19	
	Mediator of RNA polymerase II transcription subunit 8 (*)	
MED18		
Trf proximal protein		
MED9		
TRAP95		
Mediator complex subunit 28		
THRAP2		
Thyroid hormone receptor associated protein 1		
Mediator of RNA polymerase II transcription subunit 25 homologue		
TRAP 80 (*)		
CRSP9 (*)		
MED9		
Intersex like		
Thyroid hormone receptor associated protein 6		
Mediator complex subunit 28		
Similar to HSPC296		
Mediator of RNA polymerase II transcription, subunit 31 homologue		
SRB7		
Thyroid hormone receptor associated protein 1	Complex	
TRAP230 (*)		
TRAP220 (*)		
CRSP2 (*)		
Transcriptional coactivator CRSP130 (*)		
Positive cofactor 2 glutamine		
TRAP100 (*)		
Mediator of RNA polymerase II transcription subunit 25 homologue		
TRAP 80 (*)		
Vitamin D receptor interacting protein (*)		
Mediator of RNA polymerase II transcription subunit 8 (*)		

**Table S3 Continued**

Gene name	Interactors	Type of interaction
	Trf proximal protein	
	Thyroid hormone receptor associated protein 6	
	SRB7	
	CRSP9 (*)	
	Mediator complex subunit 28	
	Cyclin C	Complex
	Cyclin dependent kinase 8	
	Vitamin D receptor interacting protein (*)	
	Trf proximal protein	
	Mediator of RNA polymerase II transcription, subunit 31 homologue	
	TRAP 80 (*)	
	Mediator complex subunit 28	
	Thyroid hormone receptor associated protein 1	
	TRAP230 (*)	
	TRAP220 (*)	
	CRSP2 (*)	
	Transcriptional coactivator CRSP130 (*)	
	Thyroid hormone receptor associated protein 6	
	SRB7	
	TRAP100 (*)	
	TRAP95	
	CRSP9 (*)	
	Cyclin C	Complex
	CRSP2 (*)	
	Cyclin dependent kinase 8	
	TRAP220 (*)	
	TRAP100 (*)	
	SRB7	
	Mediator complex subunit 28	Complex
	Thyroid hormone receptor associated protein 1	
	TRAP230 (*)	
	TRAP220 (*)	
	CRSP2 (*)	
	Transcriptional coactivator CRSP130 (*)	
	TRAP100 (*)	
	TRAP95	
	Mediator of RNA polymerase II transcription subunit 25 homologue	
	TRAP 80 (*)	
	Transcriptional coactivator CRSP70 (*)	
	Vitamin D receptor interacting protein (*)	
	SRB7	
	CRSP9 (*)	
	Mediator complex subunit 28	Complex
	Surfeit 5	
	Similar to HSPC296	
	MED9	
	CRSP9 (*)	
	Mediator complex subunit 28	
	TRAP230 (*)	
	TRAP220 (*)	
	TRAP 80 (*)	
	Cyclin C	
	Cyclin dependent kinase 8	
	Mediator of RNA polymerase II transcription subunit 19	
	Mediator of RNA polymerase II transcription subunit 8 (*)	
	MED18	
	Trf proximal protein	
	MED9	
	Intersex like	
	Thyroid hormone receptor associated protein 6	
	CRSP2 (*)	Complex
	Thyroid hormone receptor associated protein 1	
	TRAP230 (*)	
	TRAP220 (*)	
	Transcriptional coactivator CRSP130 (*)	
	Positive cofactor 2 glutamine	
	Mediator of RNA polymerase II transcription subunit 25 homologue	
	Acyl-coenzyme A dehydrogenase 8	
	Actin related protein 2/3 complex subunit 2, 34kDa	

Table S3 Continued

Gene name	Interactors	Type of interaction
MED8	Mediator of RNA polymerase II transcription subunit 8 (*)	Complex
	CRSP2 (*)	
	Cyclin dependent kinase 8	
	Cyclin C	
	SRB7	Complex
	SRB7	
	Cyclin dependent kinase 8	
	Cyclin C	
	TRAP100 (*)	Complex
	Mediator of RNA polymerase II transcription subunit 25 homologue	
	TRAP 80 (*)	
	Transcriptional coactivator CRSP70 (*)	
	SRB7	Complex
	SRB7	
	TRAP220 (*)	
	CRSP2 (*)	
	Transcriptional coactivator CRSP130 (*)	
	Positive cofactor 2 glutamine	
	Mediator complex subunit 28	
	CRSP2 (*)	
	TRAP95	
	Vitamin D receptor interacting protein (*)	
	MED18	Complex
	Trf proximal protein	
	SRB7	
	Mediator of RNA polymerase II transcription, subunit 31 homologue	
	CRSP2 (*)	
	Vitamin D receptor interacting protein (*)	
	TRAP95	
	TRAP 80 (*)	
	Transcriptional coactivator CRSP130 (*)	
	TRAP100 (*)	
	Trf proximal protein	Complex
	Thyroid hormone receptor associated protein 6	
	SRB7	
	PC2	
	TRAP220 (*)	
	Mediator of RNA polymerase II transcription subunit 25 homologue	
	Cyclin dependent kinase 8	
	Intersex like	
	Thyroid hormone receptor alpha	
Mediator of RNA polymerase II transcription subunit 8 (*)	Direct	
CRSP9 (*)		
Cyclin C	Direct	
Cyclin dependent kinase 8	Direct	
RNA polymerase II transcriptional regulation mediator (*)	Direct	
Surfeit 5	Direct	
TRAP 80 (*)	Direct	
TRAP220 (*)	Direct	
TRAP230 (*)	Direct	
Transcription elongation factor B, 1	Direct	
Transcriptional coactivator CRSP34 (*)	Direct	
Transcriptional coactivator CRSP70 (*)	Direct	
Ubiquitin specific protease 49	Direct	
Thyroid hormone receptor associated protein 6	Direct	
Mediator of RNA polymerase II transcription subunit 25 homologue	Direct	
Mediator complex subunit 28	Direct	
Mediator of RNA polymerase II transcription, subunit 31 homologue	Direct	
MED9	Direct	
Similar to HSPC296	Direct	
Trf proximal protein	Direct	
Mediator of RNA polymerase II transcription subunit 19	Direct	
Ngg1 interacting factor 3 like 1 binding protein 1	Direct	
Mediator of RNA polymerase II transcription subunit 8 (*)	Direct	
Surfeit 5	Complex	
TRAP230 (*)		
TRAP220 (*)		
CRSP2 (*)		
Transcriptional coactivator CRSP130 (*)		



**Table S3 Continued**

Gene name	Interactors	Type of interaction
	Positive cofactor 2 glutamine	
	TRAP100 (*)	
	Transcriptional coactivator CRSP70 (*)	
	Cyclin dependent kinase 8	
	Cell division cycle 2 like 1	
	Vitamin D receptor interacting protein (*)	
	Mediator of RNA polymerase II transcription subunit 19	
	RNA polymerase II transcriptional regulation mediator (*)	
	MED18	
	Trf proximal protein	
	MED9	
	TRAP95	
	Mediator complex subunit 28	
	THRAP2	
	Thyroid hormone receptor associated protein 1	
	Mediator of RNA polymerase II transcription subunit 25 homologue	
	TRAP 80 (*)	
	CRSP9 (*)	
	MED9	
	Intersex like	
	Thyroid hormone receptor associated protein 6	
	Mediator complex subunit 28	
	Similar to HSPC296	
	Mediator of RNA polymerase II transcription, subunit 31 homologue	
	SRB7	
	Thyroid hormone receptor associated protein 1	Complex
	TRAP230 (*)	
	TRAP220 (*)	
	CRSP2 (*)	
	Transcriptional coactivator CRSP130 (*)	
	Positive cofactor 2 glutamine	
	TRAP100 (*)	
	Mediator of RNA polymerase II transcription subunit 25 homologue	
	TRAP 80 (*)	
	Vitamin D receptor interacting protein (*)	
	RNA polymerase II transcriptional regulation mediator (*)	
	Trf proximal protein	
	Thyroid hormone receptor associated protein 6	
	SRB7	
	CRSP9 (*)	
	Mediator complex subunit 28	
	Mediator complex subunit 28	Complex
	Surfeit 5	
	Similar to HSPC296	
	MED9	
	CRSP9 (*)	
	Mediator complex subunit 28	
	TRAP230 (*)	
	TRAP220 (*)	
	TRAP 80 (*)	
	Cyclin C	
	Cyclin dependent kinase 8	
	Mediator of RNA polymerase II transcription subunit 19	
	RNA polymerase II transcriptional regulation mediator (*)	
	MED18	
	Trf proximal protein	
	MED9	
	Intersex like	
	Thyroid hormone receptor associated protein 6	
	CRSP2 (*)	Complex
	Thyroid hormone receptor associated protein 1	
	TRAP230 (*)	
	TRAP220 (*)	
	Transcriptional coactivator CRSP130 (*)	
	Positive cofactor 2 glutamine	
	Mediator of RNA polymerase II transcription subunit 25 homologue	
	Acyl-coenzyme A dehydrogenase 8	
	Actin related protein 2/3 complex subunit 2, 34kDa	
	RNA polymerase II transcriptional regulation mediator (*)	

Table S3 Continued

Gene name	Interactors	Type of interaction
TRFP	Transcription elongation factor B, 2	Complex
	Transcription elongation factor B, 1	
	Cullin 2	Complex
	Ring-box 1	
	TRAP 80 (*)	
	Intersex like	Complex
	RNA polymerase II transcriptional regulation mediator (*)	
	Intersex like	Direct
	Thyroid hormone receptor alpha	
	Mediator of RNA polymerase II transcription subunit 8	Direct
	MED18	Direct
	Intersex like	Complex
	Surfeit 5	Complex
	TRAP230 (*)	
	TRAP220 (*)	Complex
	CRSP2 (*)	
	Transcriptional coactivator CRSP130 (*)	Complex
	Positive cofactor 2 glutamine	
	TRAP100 (*)	Complex
	Transcriptional coactivator CRSP70 (*)	
	Cyclin dependent kinase 8	Complex
	Cell division cycle 2 like 1	
	Vitamin D receptor interacting protein	Complex
	Mediator of RNA polymerase II transcription subunit 19	
	RNA polymerase II transcriptional regulation mediator (*)	Complex
	Mediator of RNA polymerase II transcription subunit 8 (*)	
	MED18	Complex
	MED9	
	TRAP95	Complex
	Mediator complex subunit 28	
	THRAP2	Complex
	Thyroid hormone receptor associated protein 1	
	Mediator of RNA polymerase II transcription subunit 25 homologue	Complex
	TRAP 80 (*)	
	CRSP9 (*)	Complex
	MED9	
	Intersex like	Complex
	Thyroid hormone receptor associated protein 6	
	Mediator complex subunit 28	Complex
	Similar to HSPC296	
	Mediator of RNA polymerase II transcription, subunit 31 homologue	Complex
	SRB7	
Thyroid hormone receptor associated protein 1	Complex	
TRAP230 (*)		
TRAP220 (*)	Complex	
CRSP2 (*)		
Transcriptional coactivator CRSP130 (*)	Complex	
Positive cofactor 2 glutamine		
TRAP100 (*)	Complex	
Mediator of RNA polymerase II transcription subunit 25 homologue		
TRAP 80 (*)	Complex	
Vitamin D receptor interacting protein (*)		
RNA polymerase II transcriptional regulation mediator (*)	Complex	
Mediator of RNA polymerase II transcription subunit 8 (*)		
Thyroid hormone receptor associated protein 6	Complex	
SRB7		
CRSP9 (*)	Complex	
Mediator complex subunit 28		
Cyclin C	Complex	
Cyclin dependent kinase 8		
Vitamin D receptor interacting protein (*)	Complex	
RNA polymerase II transcriptional regulation mediator (*)		
Mediator of RNA polymerase II transcription, subunit 31 homologue	Complex	
TRAP 80 (*)		
Mediator complex subunit 28	Complex	
Thyroid hormone receptor associated protein 1		
TRAP230 (*)	Complex	
TRAP220 (*)		
CRSP2 (*)	Complex	
Transcriptional coactivator CRSP130 (*)		

**Table S3 Continued**

Gene name	Interactors	Type of interaction
	Thyroid hormone receptor associated protein 6 SRB7 TRAP100 (*) TRAP95 CRSP9 (*) Mediator complex subunit 28 Surfeit 5 Similar to HSPC296 MED9 CRSP9 Mediator complex subunit 28 TRAP230 (*) TRAP220 (*) TRAP 80 (*) Cyclin C Cyclin dependent kinase 8 Mediator of RNA polymerase II transcription subunit 19 RNA polymerase II transcriptional regulation mediator (*) Mediator of RNA polymerase II transcription subunit 8 (*) MED18 MED9 Intersex like Thyroid hormone receptor associated protein 6 Mediator complex subunit 28 CRSP2 (*) TRAP95 Vitamin D receptor interacting protein (*) RNA polymerase II transcriptional regulation mediator (*) MED18 SRB7 Mediator of RNA polymerase II transcription, subunit 31 homologue CRSP2 (*) Vitamin D receptor interacting protein (*) RNA polymerase II transcriptional regulation mediator (*) TRAP95 TRAP 80 (*) Transcriptional coactivator CRSP130 (*) TRAP100 (*) Thyroid hormone receptor associated protein 6 SRB7 PC2	Complex
	BRCA1	Complex
<i>SURB7</i>	Basic transcription factor 3 Cyclin dependent kinase 8 RNA polymerase IIA 220 kd subunit TRK fused gene Transcription elongation factor B, 3 Cyclin dependent kinase 9 RNA polymerase IIA 220 kd subunit SMARCC1 SMARCB1 SMARCA2 SMARCC2 Cyclin C Cyclin dependent kinase 8 SWI/SNF related, matrix associated, actin dependent regulator of chromatin, subfamily d, member 1 Thyroid hormone receptor associated protein 1 TRAP230 (*) TRAP220 CRSP2 Transcriptional coactivator CRSP130 Positive cofactor 2 glutamine TRAP100 Mediator of RNA polymerase II transcription subunit 25 homologue TRAP 80 Vitamin D receptor interacting protein RNA polymerase II transcriptional regulation mediator Mediator of RNA polymerase II transcription subunit 8 Trf proximal protein Thyroid hormone receptor associated protein 6	Direct Direct Direct Direct Direct Direct Complex
		Complex

Table S3 Continued

Gene name	Interactors	Type of interaction
	CRSP9	
	Mediator complex subunit 28	
	Cyclin C	Complex
	CRSP2	
	RNA polymerase II transcriptional regulation mediator	
	Cyclin dependent kinase 8	
	TRAP220	
	TRAP100	
	Cyclin C	Complex
	Cyclin dependent kinase 8	
	Vitamin D receptor interacting protein	
	RNA polymerase II transcriptional regulation mediator	
	Trf proximal protein	
	Mediator of RNA polymerase II transcription, subunit 31 homologue	
	TRAP 80	
	Mediator complex subunit 28	
	Thyroid hormone receptor associated protein 1	
	TRAP230	
	TRAP220	
	CRSP2	
	Transcriptional coactivator CRSP130	
	Thyroid hormone receptor associated protein 6	
	TRAP100	
	TRAP95	
	CRSP9	
	Mediator complex subunit 28	Complex
	Thyroid hormone receptor associated protein 1	
	TRAP230	
	TRAP220	
	CRSP2	
	Transcriptional coactivator CRSP130	
	TRAP100	
	TRAP95	
	Mediator of RNA polymerase II transcription subunit 25 homologue	
	TRAP 80	
	Transcriptional coactivator CRSP70	
	Vitamin D receptor interacting protein	
	RNA polymerase II transcriptional regulation mediator	
	CRSP9	
	Surfeit 5	Complex
	TRAP230	
	TRAP220	
	CRSP2	
	Transcriptional coactivator CRSP130	
	Positive cofactor 2 glutamine	
	TRAP100	
	Transcriptional coactivator CRSP70	
	Cyclin dependent kinase 8	
	Cell division cycle 2 like 1	
	Vitamin D receptor interacting protein	
	Mediator of RNA polymerase II transcription subunit 19	
	RNA polymerase II transcriptional regulation mediator	
	Mediator of RNA polymerase II transcription subunit 8	
	MED18	
	Trf proximal protein	
	MED9	
	TRAP95	
	Mediator complex subunit 28	
	THRAP2	
	Thyroid hormone receptor associated protein 1	
	Mediator of RNA polymerase II transcription subunit 25 homologue	
	TRAP 80	
	CRSP9	
	MED9	
	Intersex like	
	Thyroid hormone receptor associated protein 6	
	Mediator complex subunit 28	
	Similar to HSPC296	
	Mediator of RNA polymerase II transcription, subunit 31 homologue	
	CRSP2	Complex

**Table S3 Continued**

Gene name	Interactors	Type of interaction
	RNA polymerase II transcriptional regulation mediator	
	Cyclin dependent kinase 8	
	Cyclin C	
	RNA polymerase II transcriptional regulation mediator	Complex
	Cyclin dependent kinase 8	
	Cyclin C	
	TRAP100	Complex
	Mediator of RNA polymerase II transcription subunit 25 homologue	
	TRAP 80	
	Transcriptional coactivator CRSP70	
	RNA polymerase II transcriptional regulation mediator	
	TRAP220	
	CRSP2	
	Transcriptional coactivator CRSP130	
	Positive cofactor 2 glutamine	
	Mediator complex subunit 28	Complex
	CRSP2	
	TRAP95	
	Vitamin D receptor interacting protein	
	RNA polymerase II transcriptional regulation mediator	
	MED18	
	Trf proximal protein	
	Mediator of RNA polymerase II transcription, subunit 31 homologue	Complex
	CRSP2	
	Vitamin D receptor interacting protein	
	RNA polymerase II transcriptional regulation mediator	
	TRAP95	
	TRAP 80	
	Transcriptional coactivator CRSP130	
	TRAP100	
	Trf proximal protein	
	Thyroid hormone receptor associated protein 6	
	PC2	
	TRAP100	Complex
	Mediator of RNA polymerase II transcription subunit 25 homologue	
	TRAP 80	
	Transcriptional coactivator CRSP70	
	RNA polymerase II transcriptional regulation mediator	
	TRAP220	
	CRSP2	
	Transcriptional coactivator CRSP130	
	Positive cofactor 2 glutamine	
	None	
<i>ELL3</i>	Transcription factor IIE, alpha subunit	Direct
<i>TCEA1</i>	CTD phosphatase, subunit 1	Direct
	CBF1 interacting corepressor	Direct
	RNA polymerase IIA 220 kd subunit	Direct
	EAF2	Direct
	Elongin A binding protein 1	Direct
	Hypothetical protein FLJ10006	Direct
DNA-directed RNA polymerase protein		
<i>POLR2A</i>	ABL	Direct
	ATP-dependent RNA helicase A	Direct
	Actin beta	Direct
	BAF53	Direct
	BRCA1	Direct
	BRCA1 associated ring domain 1	Direct
	CREBBP	Direct
	CTD phosphatase, subunit 1	Direct
	Caspase 10	Direct
	Cleavage and polyadenylation specificity factor 1	Direct
	Cleavage and polyadenylation specificity factor 2	Direct
	Cleavage and polyadenylation specificity factor 3	Direct
	CstF 50	Direct
	Cyclin dependent kinase 8	Direct
	EBNA2 coactivator p100	Direct
	ERCC6	Direct
	FUS	Direct
	Heterogenous nuclear ribonucleoprotein F	Direct
	Non pou domain containing octamer binding protein	Direct

Table S3 Continued

Gene name	Interactors	Type of interaction
	Pin1	Direct
	Polyglutamine binding protein 1	Direct
	Polymerase II, RNA, subunit F	Direct
	Polymerase II, RNA, subunit L	Direct
	RENT1	Direct
	RNA polymerase II elongation factor ELL	Direct
	RNA polymerase II subunit 3	Direct
	RNA polymerase II subunit D	Direct
	RNA polymerase II subunit G	Direct
	RNA polymerase IIA 25 kd subunit	Direct
	SUPT5H	Direct
	Scaffold Attachment Factor B	Direct
	Small CTD phosphatase 1	Direct
	Survival of motor neuron 1, telomeric	Direct
	TATSF1	Direct
	Transcription elongation factor A, 1	Direct
	Zinc finger protein 74	Direct
	Kallikrein 2	Direct
	ERCC5	Direct
	Transcription initiation factor IIB	Direct
	Cyclin K	Direct
	Cyclin L2	Direct
	Peptidyl prolyl isomerase G	Direct
	TAF10 RNA polymerase II TATA box binding protein TBP-associated factor 30 Kd	Direct
	XPA binding protein 2	Direct
	RNA polymerase II, polypeptide H	Direct
	MCM3 (*)	Direct
	OIP106	Direct
	SRB7	Direct
	Chorionic somatomammotropin hormone 2	Direct
	Translocation associated membrane protein 2	Direct
	Phosphorylated CTD interacting factor 1	Direct
	CDC2 related protein kinase 7	Direct
	Transcription elongation regulator 1	Direct
	Ku antigen, 80kDa	Direct
	Ccctc binding factor	Direct
	Cyclin dependent kinase 9	Direct
	BRCA1	Complex
	BRCA1 associated ring domain 1	
	SMARCA4	
	TRAP 80 (*)	
	SMARCC1	Complex
	SMARCB1	
	SMARCA2	
	SMARCC2	
	Cyclin C	
	SRB7	
	Cyclin dependent kinase 8	
	SWI/SNF related, matrix associated, actin dependent regulator of chromatin, subfamily d, member 1	
	RING3	Complex
	Cyclin dependent kinase 8	
	TRAP220 (*)	
	NELFE	Complex
	SUPT5H	
	Wolf-Hirschhorn syndrome candidate 2	
	Nucleolin	Complex
	Cyclin T1	
	PPAR gamma coactivator 1	
	Cleavage and polyadenylation specificity factor 2	
	Cyclin dependent kinase 9	
	BRCA1	Complex
	BRCA1 associated ring domain 1	
	Human capping enzyme 1	Complex
	mRNA-cap:m7G methyltransferase	
	Thyroid hormone receptor interactor 15	Complex
	Ring-box 1	
	COP9, subunit 5	
	Cullin 4A	
	COP9, subunit 3	
	DNA excision repair protein ERCC-8	

Table S3 Continued

Gene name	Interactors	Type of interaction	
<i>POLR2C</i>	COP9 signalosome subunit 4	Complex	
	Damage-specific DNA binding protein 1, 127kDa		
	G protein pathway suppressor 1		
	COP9 constitutive photomorphogenic homologue subunit 6		
	COP9 constitutive photomorphogenic homologue subunit 7A		
	COP9 constitutive photomorphogenic homologue subunit 8		
	RNA polymerase II subunit D		
	RNA polymerase IIA 25 kd subunit		
	Polymerase II, RNA, subunit F		
	RNA polymerase II subunit G		
	RNA polymerase II, polypeptide H		
	Polymerase 2, RNA, subunit K		
	Polymerase II, RNA, subunit L		
	RNA polymerase II subunit J		
	RNA polymerase II subunit I		
	BRCA1	Complex	
	RNA polymerase II subunit 2		
	RNA polymerase II subunit 3		
	CSN4		
	CSN5		
	CSN7		
	Thyroid hormone receptor interactor 15		
	Ring-box 1		
	Cullin 4A		
	COP9,subunit 3		
	DNA excision repair protein ERCC-8		
	Damage-specific DNA binding protein 1, 127kDa		
	G protein pathway suppressor 1		
	COP9 constitutive photomorphogenic homologue subunit 6		
	COP9 constitutive photomorphogenic homologue subunit 8		
	Cullin 4A	Complex	
	DNA excision repair protein ERCC-8		
	Casein kappa		
	Damage-specific DNA binding protein 1, 127kDa		
	COP9 constitutive photomorphogenic homologue subunit 6		
	COP9 constitutive photomorphogenic homologue subunit 8		
	Thyroid hormone receptor interactor 15		
	Ring-box 1		
	Chorionic somatomammotropin hormone 2		
	XPA binding protein 2		
	ATF4		Direct
	Activating transcription factor 7 interacting protein		
Myogenic factor 4			
Polymerase 2, RNA, subunit K			
Polymerase II, RNA, subunit L			
RNA polymerase II subunit D			
RNA polymerase II subunit G			
RNA polymerase IIA 25 kd subunit			
TAF15			
RNA polymerase II subunit J			
RNA polymerase II, polypeptide H			
RNA polymerase II subunit 3			
RNA polymerase II subunit 2			
RNA polymerase IIA 220 kd subunit			
Polymerase ii, rna, subunit f			
RNA polymerase II associated protein 1	Complex		
RNA polymerase II subunit 2			
RNA polymerase II subunit D			
RNA polymerase IIA 25 kd subunit			
Polymerase II, RNA, subunit F			
RNA polymerase II subunit G			
RNA polymerase II, polypeptide H			
Polymerase 2, RNA, subunit K			
Polymerase II, RNA, subunit L			
RNA polymerase II subunit J			
RNA polymerase II subunit I			
BRCA1			
RNA polymerase IIA 220 kd subunit			
RNA polymerase II subunit 2			

DNA-binding protein

Table S3 Continued

Gene name	Interactors	Type of interaction	
<i>MCM3</i>	Cyclin dependent kinase 2	Direct	
	MCM6	Direct	
	MCM7	Direct	
	Minichromosome maintenance protein 2	Direct	
	Origin recognition complex subunit 2	Direct	
	Polo like kinase	Direct	
	RNA polymerase IIA 220 kd subunit	Direct	
	MCM5	Direct	
	Minichromosome maintenance 3 associated protein	Direct	
	ORC5	Direct	
	MCM4	Direct	
	Origin recognition complex, subunit 4	Direct	
	CDC45	Direct	
	Cell division cycle 7	Direct	
	Activator of S phase kinase	Direct	
	Coiled-coil domain containing 5	Direct	
	RAD52	Direct	
	Minichromosome maintenance protein 10	Direct	
	CDC6	Direct	
	CDC5	Direct	
	Minichromosome maintenance protein 2	Complex	
	MCM7		
	MCM6		
	MCM5		
	Histone 3, H3		
	MCM4		
	<i>RUVBL1</i>	BAF53	Direct
		Catenin beta	Direct
		Plasminogen	Direct
		RuvB like 2 (*)	Direct
		C20orf20 protein	Direct
		HIV-1 Tat interacting protein, 60kDa	Complex
		Actin beta	
Mortality factor 4 like 2			
HIV-1 Tat interacting protein, 60kDa			
Inhibitor of growth family member 3			
Glioma amplified sequence 41			
Bromodomain containing 8			
350/400 kDa PCAF associated factor			
Actin-like 6A			
DMAP1			
E1A binding protein p400			
Mortality factor 4 like protein 1			
Sarcoma antigen NY-SAR-91			
EPC1			
Heat shock 70 KD protein 1A			
Ribosomal L1 domain containing 1			
C20orf20 protein			
RuvB like 2 (*)			
HIV-1 Tat interacting protein, 60kDa		Complex	
Actin beta			
Mortality factor 4 like 2			
HIV-1 Tat interacting protein, 60kDa			
Inhibitor of growth family member 3			
Glioma amplified sequence 41			
Bromodomain containing 8			
350/400 kDa PCAF associated factor			
Actin-like 6A			
DMAP1			
E1A binding protein p400			
Mortality factor 4 like protein 1			
Sarcoma antigen NY-SAR-91			
EPC1			
Heat shock 70 KD protein 1A			
Ribosomal L1 domain containing 1			
C20orf20 protein			
RuvB like 2 (*)			
Mortality factor 4 like protein 1	Complex		
Sarcoma antigen NY-SAR-91			
Inhibitor of growth family member 3			



Table S3 Continued

Gene name	Interactors	Type of interaction
RNA-binding protein <i>NCL</i>	RuvB like 2 (*)	
	EPC1	
	Enhancer of polycomb homologue 2	
	HIV-1 Tat interacting protein, 60kDa	
	Actin beta	
	HIV-1 Tat interacting protein, 60kDa	
	Glioma amplified sequence 41	
	Bromodomain containing 8	
	350/400 kDa PCAF associated factor	
	Actin-like 6A	
	DMAP1	
	E1A binding protein p400	
	RNA polymerase II subunit 5-mediating protein	Complex
	RuvB like 2 (*)	
	BCR downstream signaling 1	
	S phase kinase associated protein 2	
	NHP2 like protein 1	Complex
	Nucleolar protein NOP5	
	RuvB like 2 (*)	
	Fibrillarin	
	NHP2 like protein 1	
	NOP56	
	RNA	
	Autoantigen La (*)	Direct
	Casein kinase II, alpha 1	Direct
	Casein kinase II, alpha 2	Direct
	DNA topoisomerase I	Direct
	Glucocorticoid receptor	Direct
	Granzyme A	Direct
	Midkine	Direct
	Nucleophosmin 1	Direct
	Protein kinase C, zeta	Direct
	Telomere reverse transcriptase	Direct
	c-Myb	Direct
	p53	Direct
	Fragile X mental retardation 1 protein	Direct
	Staufen	Direct
	Calgizzarin	Direct
	PPAR gamma coactivator 1	Direct
	Protein phosphatase 2C delta isoform	Direct
	Myb-related protein A	Direct
	CD3E	Direct
Centaurin, alpha 1	Direct	
Splicing factor arginine/serine rich 12	Direct	
FXR1	Complex	
FXR2		
Cytoplasmic FMR1 interacting protein 1		
Cyclin T1	Complex	
PPAR gamma coactivator 1		
Cleavage and polyadenylation specificity factor 2		
RNA polymerase IIA 220 kd subunit		
Cyclin dependent kinase 9		
TATSF1	Complex	
Polymerase II, RNA, subunit F		
SUPT5H		
60 kDa Ro protein	Complex	
Autoantigen La (*)		
GAJ/ Bop1	Complex	
NIFK		
NNP1		
Ribosomal protein L3		
Ribosomal protein L8		
YTM1P		
Cell division cycle 2 like 2		
Fibronectin 1		
Ribosomal protein S3a		
Ribosomal protein L4		
Ribosomal phosphoprotein large P0		
DDX5		

Table S3 Continued

Gene name	Interactors	Type of interaction
PRPF31 SNRPD2	Ribosomal protein L7a	
	Tubulin alpha 1	
	Peptidyl prolyl cis/trans isomerase nima interacting, 4	
	DDX1	
	Ribosomal protein S9	
	Ribosomal protein L21	
	Ribosomal protein L17	
	Ribosomal protein L6	
	Ribosomal protein L26	
	Ribosomal protein L7	
	P160	
	Growth arrest specific protein 8	
	Pescadillo homologue 1	
	C20ORF1 protein	
	DDX24	
	DDX21	
	GTP binding protein 4	
	NOP56	
	Ribosomal protein L10a	
	Ribosomal protein S3	
	Nucleolar protein NOP5	
	Nucleophosmin 1	Complex
	Switch associated protein 70	
	ADP ribosyl transferase	
	None	
	EGF receptor	Direct
	Small nuclear ribonucleoprotein polypeptide D1	Direct
	Survival of motor neuron 1, telomeric	Direct
	Small nuclear ribonucleoprotein polypeptide D2	Direct
	Syntaxin binding protein 2	Direct
	SMN interacting protein 1	Direct
	Small nuclear ribonucleoprotein polypeptide F	Direct
	DDX20	Direct
	Gemin 5	Direct
	Gemin 6	Direct
	LSM2	Direct
	LSM6	Direct
	Gemin 4	Direct
	Survival of motor neuron 2, centromeric	Direct
	Syntaxin binding protein 3	Direct
	Methylosome protein 50	Direct
	HIV-1 Tat interacting protein, 60kDa	Direct
	Gemin 7	Direct
	Small nuclear ribonucleoprotein polypeptide E	Complex
	Small nuclear ribonucleoprotein polypeptide D3	
	Small nuclear ribonucleoprotein polypeptide D1	
	Small nuclear ribonucleoprotein polypeptide F	
Small nuclear ribonucleoprotein polypeptide G		
Splicing factor, arginine/serine-rich 7		
Programmed cell death 7		
Chromosome 16 open reading frame 33		
Small nuclear ribonucleoprotein polypeptide E	Complex	
U2AF1L2		
Small nuclear ribonucleoprotein polypeptide D3		
Small nuclear ribonucleoprotein polypeptide D1		
DDX15		
Small nuclear ribonucleoprotein polypeptide F		
Small nuclear ribonucleoprotein polypeptide G		
Splicing factor 3B subunit 1		
Pre mRNA branch site protein p14		
Programmed cell death 7		
U11/U12 snRNP 35K		
p175	Complex	
CD69 antigen		
Small nuclear ribonucleoprotein polypeptide E		
Small nuclear ribonucleoprotein 70 kD		
CD2		



Table S3 Continued

Gene name	Interactors	Type of interaction
	U2AF35 U2AF65 Splicing factor, arginine/serine rich 1 Small nuclear ribonucleoprotein polypeptide D3 Small nuclear ribonucleoprotein polypeptide D1 DDX15 SMN related protein U2 small nuclear ribonucleoprotein B U2A prime Small nuclear ribonucleoprotein polypeptide F Small nuclear ribonucleoprotein polypeptide G High mobility group protein 20B Heat shock protein, 75 kDa Splicing factor, 45 kd CHERP PUF60 SF3b10 SF3b14b SPF31 SR140 hPrp5p Heat shock 60 KD protein 1 Small nuclear ribonucleoprotein polypeptide E SNRPB U2AF35 U2AF65 Splicing factor 3A, subunit 2 Splicing factor, arginine/serine rich 1 Small nuclear ribonucleoprotein polypeptide D3 Small nuclear ribonucleoprotein polypeptide D1 DDX15 SMN related protein U2 small nuclear ribonucleoprotein B U2A prime Small nuclear ribonucleoprotein polypeptide F Small nuclear ribonucleoprotein polypeptide G High mobility group protein 20B Heat shock protein, 75 kDa Splicing factor 3 subunit 1 Splicing factor, 45 kd Pre mRNA branch site protein p14 Spliceosome associated protein 145 Splicing factor 3A, subunit 3 Splicing factor 3B, subunit 3 Splicing factor 3B subunit 4 CHERP	Complex
Serine/threonine kinase protein Serine/threonine phosphatase protein <i>PPP2R1A</i>	Glutamate receptor ionotropic, N-methyl D-aspartate 1 Heat-shock transcription factor 2 NMDAR2D Protein phosphatase 2, regulatory subunit B (B56), alpha Protein phosphatase 2, regulatory subunit B', alpha Protein phosphatase 5 catalytic subunit Protein phosphatase 2A regulatory subunit, 48kD Solute carrier family 6 (neurotransmitter transporter, noradrenalin), member 2 Importin 9 Guanine nucleotide binding protein, alpha 12 CDC42 Ubiquitin-specific protease 9 P160 Cytoplasmic FMR1 interacting protein 1 Ubiquitin specific protease 7 KIAA0802 Dedicator of cytokinesis 7 Rho guanine nucleotide exchange factor 2 Protein kinase C, iota type TGFB1 induced anti apoptotic factor 1 Hypothetical protein KIAA0889	Direct Direct Direct Direct Direct Direct Direct Direct Direct Direct Complex

Table S3 Continued

Gene name	Interactors	Type of interaction
Translation regulator protein <i>EEF1B2</i>	Cytoplasmic FMR1 interacting protein 2	
	SMARCA4	
	Paraneoplastic antigen MA1	
	Paraneoplastic antigen ma2	
	Ring finger protein 41	
	Protein phosphatase 2A, catalytic subunit, beta isoform	
	14-3-3 zeta	
	14-3-3 Eta (*)	
	Chromosome 6 open reading frame 69	
	Histidyl-tRNA synthetase	Direct
	Casein kinase II, alpha 2	Direct
	Casein kinase II, alpha 1	Direct
	Alanyl tRNA synthetase	Direct
Elongation factor 1 alpha 1	Complex	
Eukaryotic translation elongation factor 1,delta		
Eukaryotic translation elongation factor 1 gamma		
Valyl tRNA synthetase 2	Complex	
Elongation factor 1 alpha 1		
Eukaryotic translation elongation factor 1,delta		
Elongation factor G 1		
Auxiliary transport protein <i>GDI2</i>	RAB8	Direct
	Ras associated protein RAB9	Direct
	Ras associated protein Rab2	Direct
	Ras associated protein Rab4	Direct
	Ras related protein Rab 5A	Direct
	Ras family, member rab 11A	Direct
Receptor signalling complex scaffold protein <i>YWHAE</i>	ASK1	Direct
	Ataxin 1	Direct
	BCL2 antagonist of cell death	Direct
	CDC 25A	Direct
	CDC 25B	Direct
	Calmodulin 1	Direct
	Cyclin dependent kinase inhibitor 1B	Direct
	DNA topoisomerase II alpha	Direct
	IGF-1 receptor	Direct
	IRS 1	Direct
	IRS2	Direct
	Keratin 18	Direct
	Kinesin family member 1C	Direct
	MAP3K10	Direct
	Mitogen-activated protein kinase kinase kinase 3	Direct
	NGFR associated protein 1	Direct
	PCTAIRE protein kinase 1	Direct
	Potassium channel, voltage gated subfamily H, member 2	Direct
	RAF1	Direct
	Regulator of G protein signaling 3	Direct
	SHC	Direct
	Synuclein alpha	Direct
	TGF beta 1	Direct
	Tafazzin	Direct
	Tuberin	Direct
	Vimentin	Direct
	Zinc finger protein A20	Direct
	c-Src	Direct
	Retinitis pigmentosa GTPase regulator	Direct
	Histone deacetylase 4	Direct
	RAS inhibitor 1	Direct
	Nude like protein	Direct
	Ras protein specific guanine nucleotide releasing factor 1	Direct
Histone deacetylase 5	Direct	
TAZ	Direct	
MAP3K2	Direct	
Poly A polymerase alpha	Direct	
Rho guanine nucleotide exchange factor 2	Direct	
REM1	Direct	
Rho guanine nucleotide exchange factor	Direct	

Table S3 Continued

Gene name	Interactors	Type of interaction
SPIN YWHAQ	Tuberous sclerosis 1 gene	Direct
	Nuclear receptor corepressor 2	Direct
	Cell division cycle 2 like 1	Direct
	Heat shock 70 KD protein 1A	Complex
	HSP90A	
	14-3-3 zeta	
	14-3-3 Beta	
	Insulin receptor substrate 4	
	WD repeat domain 6	
	Mitogen-activated protein kinase kinase kinase 3	Complex
	14-3-3 zeta	
	14-3-3 Beta	
	14-3-3 Eta (*)	
	14-3-3 gamma	
	14-3-3 theta	
	p53 and DNA damage regulated 1	
	CDC37	
	Mortalin 2	
	HSPCAL3	
	HSP90B	
	EMK1	
	MAP2K5	
	Prefoldin 2	
	None	
	CDC 25B	Direct
	Calpain 3	Direct
	Follicle stimulating hormone receptor	Direct
	Heat shock 70 KD protein 1A	Direct
	NIF3L1	Direct
	14-3-3 theta	Direct
	B-Raf	Direct
	Fgr	Direct
	CBL	Direct
	6-phosphofructo-2 kinase/fructose-2,6-biphosphatase 2	Direct
	Telomere reverse transcriptase	Direct
	Tuberin	Direct
	BAX	Direct
	NFAT1	Direct
	Casein kinase 1, alpha 1	Direct
	Myocyte specific enhancer factor 2D	Direct
	Cyclin dependent kinase inhibitor 1B	Direct
	Mtor	Direct
	Kinesin light chain 2 like	Direct
	Uncoupling protein 2	Direct
	Uncoupling protein 3	Direct
	SH3 domain binding protein 2	Direct
	Regulator of G protein signaling 3	Direct
	ASK1	Direct
	Regulator of G protein signaling 7	Direct
	Tubulin, alpha 2	Direct
	MAGOH	Direct
	Phosphatidylinositol 3-kinase, catalytic beta	Direct
Ubiquitin specific protease 8	Direct	
BCL2 antagonist of cell death	Direct	
IcIn-binding protein, 72 kd	Direct	
3 Phosphoinositide dependent protein kinase 1	Direct	
Protein kinase C, mu	Direct	
Lysosomal trafficking regulator	Direct	
Keratin 9	Direct	
DDX48	Direct	
Heat shock 70 kDa protein 8	Direct	
Kinesin family member 5B	Direct	
NFAT3	Direct	
Yes associated protein	Direct	
Phosphatidylinositol 4 kinase catalytic beta polypeptide	Direct	
Methylosome protein 50	Direct	
REM1	Direct	
Tuberous sclerosis 1 gene	Direct	
Calcineurin binding protein 1	Direct	
Cell division cycle 2 like 1	Direct	

Table S3 Continued

Gene name	Interactors	Type of interaction
	HS1 binding protein	Direct
	B-Raf	Complex
	RAP1 GTPase activating protein 1	
	Mitogen-activated protein kinase kinase kinase 3	Complex
	14-3-3 zeta	
	14-3-3 Beta	
	14-3-3 epsilon	
	14-3-3 Eta (*)	
	14-3-3 gamma	
	p53 and DNA damage regulated 1	
	CDC37	
	Mortalin 2	
	HSPCAL3	
	HSP90B	
	EMK1	
	MAP2K5	
	Prefoldin 2	
<i>AP3S1</i>	IRS 1	Direct
	SCARB2	Direct
	Adaptor related protein complex 3, beta-2 subunit	Direct
	Clathrin adaptor complex AP3, sigma 3B subunit	Direct
	Solute carrier family 30, member 3	Direct
	Adaptin, delta	Direct
	Adaptin, delta	Complex
	Centaurin gamma 2	
Transmembrane receptor protein tyrosine kinase protein <i>FGFR2</i>	Calcium channel voltage dependent, L type alpha 1D subunit	Direct
	Fibroblast growth factor 1	Direct
	Fibroblast growth factor 5	Direct
	Fibroblast growth factor 7	Direct
	Phospholipase C, gamma 1	Direct
	Fibroblast growth factor 2	Direct
	Integrin alpha 5	Direct
	Fibroblast growth factor receptor 2	Direct
	Fibroblast growth factor 9	Direct
	Fibroblast growth factor 10	Direct
	CBL	
	Lyn	
	Fyn	Complex
Lipid kinase protein <i>PIP5K2B</i>	Tumour necrosis factor receptor 1	Direct
	Phosphatidylinositol-4-phosphate 5-kinase type II beta	Direct
	None	
<i>PIP5K2C</i>		
Heterotrimeric G-protein GTPase protein <i>GNB4</i>	Guanine nucleotide binding protein, gamma 13	Direct
	Guanine nucleotide binding protein, gamma 12	Direct
Guanyl-nucleotide exchange factor protein <i>ARHGEF4</i>	APC	Direct
	RhoA	Direct
	Catenin beta	Complex
	APC	
Calcium-binding protein (signal transduction) <i>S100A8</i>	Neutrophil cytosolic factor 2	Direct
	S100 Calcium binding protein A9	Direct
	Carcinoembryonic antigen related cell adhesion molecule 3	Direct
	S100 Calcium binding protein A8	Direct
<i>S100A9</i>	S100 Calcium binding protein A8	Direct
	S100 Calcium binding protein A9	Direct
Enzyme: dehydrogenase <i>GAPDH</i>	Actin beta	Direct
	Amyloid beta A4 protein	Direct
	Calcyclin	Direct
	Solute carrier family, member 1	Direct
	Glyceraldehyde 3 phosphate dehydrogenase	Direct
	Huntingtin	Direct
	Diphosphoglycerate mutase	Direct
	Protein kinase C, iota type	Direct
	Phosphoglycerate kinase 1	Direct
	Androgen receptor	Direct

Table S3 Continued

Gene name	Interactors	Type of interaction
<i>MDH2</i>	Ataxin 1	Direct
	Dynein light chain 1	Direct
	Phospholipase D2	Direct
	Metabotropic glutamate receptor 1	Direct
	Protein disulfide isomerase A2	Direct
	HIV-1 Tat interacting protein, 60kDa	Direct
	SIAH-1	Direct
	Citrate synthase	Direct
	Fumarase	Direct
	Glutamate oxaloacetate transaminase, mitochondrial	Direct
	Malate dehydrogenase mitochondrial	Direct
	NADH ubiquinone oxidoreductase Fe-S protein 1	Direct
	Pyruvate carboxylase	Direct
Enzyme: synthase <i>PTS</i>	BRG1 associated factor,180 KD	Direct
	6 pyruvoyl tetrahydrobiopterin synthase	Direct
	Fibronectin type III domain containing 5	Direct
	Protein kinase cGMP dependent Type II	Direct
Unknown <i>LSM14</i> <i>DRG1</i>	None	
	Leukemia lymphoid 1	Direct
	T cell acute lymphocytic leukemia 1	Direct
<i>HCCA2</i>	Serine/threonine protein kinase 38	Direct
	NDRG family member 2	Direct
<i>C20orf11</i> <i>SMAD9</i>	None	
	Activin A receptor, type I	Direct
	BTG2	Direct
	Bullous pemphigoid antigen 1	Direct
	HEY1	Direct
	Leucyl cystinyl aminopeptidase	Direct
	Ribosome binding protein 1	Direct
	Small nuclear ribonucleoprotein 70 kD	Direct
	Upstream regulatory element binding protein 1	Direct
	TOB1	Direct
	SMAD4	Direct
	SMAD, mothers against DPP homologue 2 (Drosophila)	Direct
	Low density lipoprotein receptor related protein 5	Direct
	MLL2	Direct
	Hypothetical protein FLJ32214	Direct
	Splicing factor 3B subunit 1	Direct
	Potential carboxypeptidase like protein X2	Direct
	Exophilin 5	Direct
	Regulatory factor X 1	Direct
	MAN antigen 1	Direct
	Zinc finger and SCAN domain containing 4	Direct
	E4F transcription factor 1	Direct
	Hypothetical protein KIAA0226	Direct
	SECIS binding protein 2	Direct
	Aryl hydrocarbon receptor nuclear translocator	Direct
	Chorionic somatomammotropin hormone 1	Direct
	Zinc finger protein 484	Direct
	Zinc finger protein 587	Direct
	Rho GTPase activating protein 9	Direct
	Plakophilin 2	Direct
	Proline glutamic acid leucine-rich protein 1	Direct
	Granulin	Direct
	Hypothetical protein FLJ10747	Direct
	ASH2 like	Direct
	Prosaposin	Direct
	KIAA0372	Direct
	N-acetylglucosamine kinase	Direct
	BiP associated protein	Direct
	TID 1	Direct
	Dickkopf 1	Direct
	Poly(A) binding protein 4	Direct
	Plectin 1	Direct
	Lipocalin 7	Direct
	Ubiquitously transcribed TPR protein on the X chromosome	Direct
	EIF3S8	Direct
	Protein phosphatase 2 regulatory subunit B (B56) epsilon	Direct



Table S3 Continued

Gene name	Interactors	Type of interaction
	KIAA0804	Direct
	RAN binding protein 9	Direct
	Hairy/enhancer-of-split related with YRPW motif-like	Direct
	SH2 domain binding protein 1	Direct
	MLLT2	Direct
	XPA binding protein 2	Direct
	TRIM29	Direct
	Minichromosome maintenance 3 associated protein	Direct
	Peroxisome proliferator activated receptor, delta	Direct
	EIF3S5	Direct
	Bromodomain adjacent to zinc finger domain 1A	Direct
	Zinc finger protein 592	Direct
	Hypothetical protein FLJ20313	Direct
	Mannosidase alpha class 1A member 2	Direct
	OTUBAIN 1	Direct
	FLJ10808 Protein	Direct
	Fibronectin 1	Direct
	LIM domain only 4	Direct
	Fodrin beta	Direct
	Ubiquilin 1	Direct
	Hypothetical protein FLJ13910	Direct
	Phosphorylase kinase liver alpha 2 subunit	Direct
	DnaJ homologue subfamily C member 7	Direct
	Tubulin specific chaperone D	Direct
	14-3-3 theta	Direct
	Ferritin light chain	Direct
	Patatin like phospholipase domain containing 2	Direct
	Cisplatin resistance associated	Direct
	PI3 kinase related kinase SMG1	Direct
	Ubiquitin protein ligase E3A	Direct
	DIAPH3	Direct
	Cytochrome P450, subfamily XIA	Direct
	SKD3	Direct
	Zinc finger protein 83	Direct
	MGAT1	Direct
	Adaptor related protein complex 2 alpha 1 subunit	Direct
	ASB2	Direct
	Alpha mannosidase B	Direct
	Smooth muscle cell associated protein 1	Direct
	Methyl CpG binding domain protein 1	Direct
	SMAD3	Direct
	Pregnancy associated plasma protein A	Direct
	GlutaminyI tRNA synthetase	Direct
	Ataxin 1 ubiquitin like interacting protein	Direct
	Chromosome 9 open reading frame 13	Direct
	Pirin	Direct
	Stromal antigen 1	Direct
	Centrosome protein 4	Direct
	Limbin	Direct
	CXXC finger 5	Direct
	Thyroid hormone receptor interactor 12	Direct
	Actin beta	Direct
	Zinc finger protein 557	Direct
	Destrin (actin depolymerizing factor)	Direct
	ARID1B	Direct
	Mannosidase, alpha, class 1C, member 1	Direct
	Eukaryotic translation initiation factor 3, subunit 6 48kDa	Direct
	Chondroitin polymerizing factor	Direct
	Ring finger protein 123	Direct
	Elongation factor 1A binding protein	Direct
	Proteasome 26S subunit, non ATPase 8	Direct
	FLI1	Direct
	C10orf2 protein	Direct
	SMAD interacting protein 1	Direct
	Telomeric repeat binding factor NIMA-interacting 1	Direct

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