by dormant primordial follicles (PMF) which are necessary to maintain female reproductive function. There is a continuous repression of PMF activation in early growing follicle through the balance between factors activating the initiation of follicular growth, mainly actors of the phosphatidylinositol-3-kinase (PI3K) signaling pathway, and inhibiting factors such as Anti-Müllerian Hormone (AMH). Any alteration of this equilibrium may induce early follicle depletion and subsequent infertility. Cyclophosphamide (Cy) one of the alkylating agents commonly used for treating breast cancer is able to trigger PMF activation further leading to premature ovarian insufficiency. Preventing chemotherapy-induced ovarian dysfunction might represent an option for preserving optimal chances of natural or medically assisted conceptions after healing.

We showed in a model of Cy-treated pubertal mice, that AMH administration was able to restrain PMF depletion by counting the total PMF number within mouse ovaries. Moreover, the PI3K signaling pathway was evaluated following Cy administration with and without AMH injection. We showed that AMH decreased the phosphorylation of FOXO3A, a transcription factor of PMF activation and induced its nuclear translocation. Altogether, the results support a protective role of AMH against Cy-induced follicular loss. To better understand AMH action in the ovary, we investigated the molecular mechanism to explain the protective effect of this hormone on the PMF pool. It has been reported that autophagy, a lysosomal degradative ubiquitous process implicated in cellular homeostasis, was involved in both ovarian follicular death and survival mostly by PI3K pathway (Gawriluk et al. Reproduction 2011 141, 759–765). We show in mice that Cy inhibits autophagy in the ovary while AMH induces autophagy. *In vivo* analysis of autophagic flux is currently in progress to dissect this process more finely. Interestingly, FOXO3A was shown to be related to autophagy activation. To investigate the role of FOXO3A in AMH-induced autophagy further, we analyzed mRNA and protein expression of autophagy-related genes controlled by FOXO3A, including BECLIN-1, ATG12, ULK1, BNIP3, GABARAP, and LC3B. These findings establish a close relationship between AMH and autophagy to protect PMF stockpile and to limit follicular depletion induced by Cy.

Adipose Tissue, Appetite, and Obesity

NEURAL MECHANISMS OF OBESITY

Growth Hormone-Releasing Hormone (GHRH) Antagonists Stimulate Feeding in Mice

Sheila Leone, MD[1], Lucia Recinella, PharmD, PhD[1], Annalisa Chiavaroli, PharmD, PhD[1], Giustino Orlando, PharmD, PhD[1], Claudio Ferrante, PharmD, PhD[1], Iacopo Gesmundo, PhD[2], Riccarda Granata, PhD[2], Renzhi Cai, PhD[3], Wei Sha, BS[4], Andrew V. Schally, MD,PHD[3], Luigi Brunetti, MD,PhD[1].

[1]G d'Annunzio University, Department of Pharmacy, Chieti, Italy, [2]University of Turin, Department of Medical Sciences, Turin, Italy, [3]Veterans Affairs Medical Center, Endocrine, Polypeptide and Cancer Institute, Miami, FL, USA, [4]University of Miami, Department of Pathology, Miami, FL, USA.

SAT-603

Growth hormone-releasing hormone (GHRH) is a hypothalamic neuropeptide which stimulates the synthesis and secretion of growth hormone (GH) in pituitary gland. GHRH was also found to modulate food intake in mammals. MIA-690 is a synthetic GHRH antagonist of the Miami (MIA) series with potent antitumor effects. To date, its role in hypothalamic feeding modulation has not been evaluated. In the present study, we aimed to investigate the effects of chronic MIA-690 administration on feeding behavior, locomotor activity and hypothalamic dopamine (DA), norepinephrine (NE), serotonin (5-hydroxytriptamine, 5-HT), orexigenic peptides [agouti-related peptide (AgRP) and neuropeptide Y (NPY)] and anorexigenic peptides [cocaine and amphetamine-regulated transcript (CART) and proopiomelanocortin (POMC)] activity.

Adult C57/BL6 mice were treated daily for 4 weeks by subcutaneous administration of (5 μg) MIA-690 or vehicle solution. Food intake and body weight were recorded every 4 days throughout the study. Immediately after the last injection, locomotor activity in the home cage was recorded, and thereafter animals were sacrificed. Visceral, subcutaneous and brown fat depots were quickly excised and weighed. Hypothalamus was also dissected for evaluating gene expression of AgRP, NPY, CART and POMC by real-time reverse transcription polymerase chain reaction. In addition, hypothalamic DA, NE and 5-HT levels were measured by high performance liquid chromatography (HPLC) coupled to electrochemical detection.

Our findings show that administration of MIA-690 increased food intake and body weight, without affecting locomotor activity. No difference was observed in visceral, subcutaneous and brown fat mass in animals treated with MIA-690 or vehicle. As for neuromodulatory effects, a significant increase of AgRP gene expression and NE levels, along with a reduction of 5-HT levels were found after MIA-690 treatment. On the other hand, we did not observe any alteration in NPY, POMC and CART gene expression, as well as DA levels, following MIA-690 administration.

In conclusion, chronic peripheral administration of MIA-690 could play an orexigenic role paralleled by increased body weight. The stimulation of feeding could be mediated, at least in part, by increased AgRP gene expression and NE levels and decreased 5-HT levels, in the hypothalamus.

Thyroid

THYROID NEOPLASIA AND CANCER

Pre-Operative Calcitonin Value as a Predictive Factor of Cancer Related Death in Sporadic Medullary Thyroid Carcinoma

Antonio Matrone, MD, Virginia Cappagli, MD, Delio Stefani Donati, MD, Alessandro Prete, MD, Laura Valerio, MD, Carlotta Giani, MD, Valeria Bottici, MD, David Viola, MD, Laura Agate, MD, Eleonora Molinaro, MD, Paolo Vitti, Professor, Rossella Elisei, Professor.

Department of Clinical and Experimental Medicine, Unit of Endocrinology 1, University Hospital of Pisa, Pisa, Italy.

OR21-01

Introduction: Medullary thyroid carcinoma (MTC) is a rare tumor, it originates from the C cells producing calcitonin (CT) and can occur as sporadic or associated to germline RET mutation. The initial treatment is represented by total thyroidectomy associated with central