shown impairment of phosphorylation in several intracellular signaling pathways following CLP, a well-validated murine model of sepsis (2). Phosphorylation of tyrosine in IRS-2 is essential for functional insulin signaling in hepatocytes (3). Therefore the aim of this study was to investigate the effects of CLP on IRS-2 phosphorylation.
**Hypothesis:** CLP attenuates phosphorylation of IRS-2.
**Methods:** All studies were approved by the Feinstein IACUC and conformed to ARRIVE guidelines. CLP was performed on C57Bl6 mice. Before CLP, animals were identified for sacrifice at specific post-procedure time points. To stimulate phosphorylation of IRS-2, insulin was injected in control and CLP mice at 24 and 48 hours post CLP. Following sacrifice, protein was isolated from liver tissue. Protein abundance was determined using immunoblotting. The detection of the phosphorylated form of these proteins was determined by enzyme-linked immunosorbent assay (ELISA) with a phospho-insulin receptor antibody. Statistical significance was determined using ANOVA for repeated measures with a Sidak post-hoc correction.
**Results:** Relative to the control, tyrosine phosphorylation of IRS-2 was significantly ($p<0.05$) reduced at 24 and 48 hours following CLP.
**Conclusions:** Tyrosine phosphorylation of hepatic IRS2 is attenuated at early time points following CLP. These results are consistent with other studies examining the effects of CLP on intra-cellular signal transduction pathways (1). Further, these results provide evidence that changes in the insulin signaling transduction underlie CLP-induced "insulin resistance".
**References:** (1) Abcejo et al., Crit Care Med. 2009;37(5):1729-1734. (2) van den Berghe et al, NEngl J Med. 2001;345(19):1359-1367. (3) Valverde et al., Diabetes 2003 Sep; 52(9): 2239-2248.

# Steroid Hormones and Receptors

## STEROID BIOLOGY AND ACTION

### *HNRNPA2B1 Mediates Endocrine-Sensitivity and Alters PSAT1 in Breast Cancer Cells*

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Higher expression of the RNA binding protein HNRNPA2B1 (Heterogeneous Nuclear Ribonucleoprotein A2/B1), a reader of the N(6)-methyladenosine (m6A) mark in transcribed RNA, is found in endocrine-resistant, estrogen receptor (ERα)+ LCC9 and LY2 breast cancer cells derived from MCF-7 endocrine-sensitive luminal A cells (1). HNRNPA2B1 interacts with DGCR8 in the DROSHA complex to promote processing of pri-miRNAs to pre-miRNAs. We identified HNRNPA2B1-regulated miRNAs by RNA seq and target pathways, including serine family amino acid metabolic processes, TGFβ signaling, response to estrogen, and cell junction by MetaCore enrichment pathway analysis (1). Stable 4.5-fold overexpression of HNRNPA2B1 in MCF-7 cells (MCF-7-A2B1 cells) results in ablation of growth inhibition by 4-hydroxytamoxifen (4-OHT) and fulvestrant. This was not due to loss or decrease of ERα; in fact, ERα was increased ~ 1.6-fold. Conversely, transient knockdown of HNRNPA2B1 expression in LCC9 and LY2 cells sensitized the cells to growth inhibition by 4-OHT and fulvestrant, without changing *ESR1* expression. MCF-7-A2B1 cells showed increased migration, reduced E-cadherin and increased vimentin, suggestive of EMT; however, they exhibited reduced clonogenic survival. Follow-up on the identification of HNRNPA2B1-miRNA regulation of the serine pathway revealed higher expression of phosphoglycerate dehydrogenase (PHGDH) and phosphoserine aminotransferase (PSAT1) transcripts and proteins in LCC9, LY2, and MCF-7-A2B1 compared to MCF-7 cells. We identified two miRNAs, miR-424-5p and miR-145-5p downregulated in MCF-7-A2B1 cells that directly targeted the PSAT1 3'UTR in dual luciferase assays. Lower miR-424-5p and miR-145-5p in endocrine-resistant LCC9 and LY2 correlate with increased PSAT1 and higher PSAT1 is associated with reduced overall and metastasis-free survival in breast cancer patients. Overall, our data suggest a role for increased HNRNPA2B1 in tamoxifen-resistance. **Reference:** (1) Klinge CM, Piell KM, Tooley CS, Rouchka EC. HNRNPA2/B1 is upregulated in endocrine-resistant LCC9 breast cancer cells and alters the miRNA transcriptome when overexpressed in MCF-7 cells. Sci. Rep. 2019; 9:9430.

# Thyroid

## THYROID DISORDERS CASE REPORTS I

### *Thyrotoxic Periodic Paralysis in Adolescence Patient a Case Report and Literature Review*

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**Background:** Thyrotoxic periodic paralysis (TPP) is an uncommon disorder characterized by acute flaccid paralysis due to hypokalemia. It is diagnosed primarily in Asian adult males and is rare in children and adolescents. Here we report an adolescent male patient of Vietnamese descent who presented to the emergency department with an episode of syncope, muscle weakness, and shortness of breath one day after the initiation of methimazole treatment for Graves' disease. The laboratory revealed significant hypokalemia. In this report we also included and summarized the reported cases of TPP in adolescent patients since 1997.
**Clinical Case:** A 17-year-old Vietnamese American male who was recently diagnosed with Graves' disease presented to the emergency department after an episode of syncope, muscle weakness, and difficulty breathing. Two months previously, he began having episodes of tachycardia. He was diagnosed with hyperthyroidism with a TSH of 0.007 mIU/mL and free T 4 > 7 ng/dL (0.8-1.9). He was subsequently evaluated by Cardiology and started on atenolol. He was then seen by Endocrinology 5 days after and started on methimazole 15 mg twice daily. On the next morning after starting methimazole, he reported feeling weak and passed out. His father had found him on the floor, weak and unable to move, approximately 30 minutes after his father "heard a thud upstairs". The patient recalled that his legs gave out and he "hitting his face on a table". In the emergency