Translatome of the follicle-stimulating hormone receptor, in primary rat Sertoli cells.

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G protein-coupled receptors (GPCR) indirectly regulate gene transcription, but little is known about their role in mRNA translation. Regulatory mechanisms acting at the level of translation allow the cell to respond in a few minutes to subtle changes in the extracellular *milieu*. For example, variations of the follicle-stimulating hormone (FSH) input could lead to regulations occurring at the translational level and ultimately fine-tune Sertoli cell (SC) protein content in the male gonad.

Our group has previously shown that FSH binding to the FSHR targets mRNA-specific translation of *c-fos* and *vegf* [1], indicating FSH-dependent translational regulation of preexisting mRNA pools in SC. To further explore this point and assess to what extent the whole translatome is affected by FSH, we combined polysome profiling[2] by sucrose density gradient fractionation with RNA-seq analysis in rat primary SC exposed to FSH for 90 min. Comparison of normalized polysomal fractions in stimulated *vs* non-stimulated cells led to identifying more than two thousands mRNA whose translation goes significantly up or down in response to FSH. From these mRNA, Ingenuity pathway analysis (IPA) identified 30 mRNA which encode specific testis markers. Importantly, detailed analysis of canonical pathways highlighted that several components belonging to 4 major RFSH-dependent signaling pathways (Gαs, cAMP, Gαq, mTOR) were co-translated in response to FSH. In contrast, upon 90 min of FSH stimulation, only 244 mRNA were regulated at the transcriptome (pooled of free mRNA, 80S-bound and polysomal mRNA) level.

To our knowledge, this study reports the first GPCR-dependent translatome analyzed at the systems level. We expect that it will eventually provide insights onto the molecular mechanisms whereby this class of receptor physiologically controls cell phenotype.

[1] Musnier and Leon, 2012.Mol.Endocrinol, 26(6):669-680.

[2] Aneichyk et al., 2013. BMC Genomics, 1471-2164-14-844.