

RGS19 up-regulates Nm23-H1/2 expression via stimulating multiple transcriptional factors

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The Nm23 gene family is comprised of ten genes that are involved in a variety of physiological and pathological processes ranging from cell proliferation, differentiation, apoptosis, cell cycle regulation, tumorigenesis to metastasis. Nm23-H1 and H2 are the most widely studied isoforms due to their ability to suppress metastasis. Loss or reduced expression of Nm23-H1/2 is often associated with aggressive metastatic potential in different types of tumors. Conversely, elevated expression of Nm23-H1/2 has been shown to suppress metastasis. We have recently shown that both Nm23-H1 and H2 are up-regulated by RGS19 (regulator of G-protein signaling 19, a GTPase activating protein for $G\alpha_{i/o}$ and $G\alpha_q$ subunits) in multiple cell types. However, the mechanism involved in RGS19-induced transcriptional regulation of Nm23 remains unknown. By means of *in silico* comparison of promoter sequences and luciferase reporter assays, we showed that the transcription factor AP-1 might be involved in the up-regulation of Nm23-H1/2 by RGS19. Both transient and stable expressions of RGS19 in HEK293 cells are able to stimulate the pAP-1-luc reporter. Since Nm23-H1 and H2 do not appear to utilize identical signaling partners, we have identified sixteen amino acids on the exposed surfaces of Nm23-H1 that are different from H2. To examine if these residues are responsible for specific protein-protein interactions between Nm23-H1/2 and diverse binding partners, we have constructed seven mutants with double or triple mutations that may alter the specificity of signaling. These Nm23 mutants will be characterized for their ability to regulate tumorigenesis and metastasis (Supported by HKUST 663110 and RPC11SC07).

Development of an aptamer-based biosensing system for measuring luteinizing hormone pulsatility for infertility treatment

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Normal fertility in human involves a highly orchestrated signal communication between the hypothalamic-pituitary-gonadal. The pulsatile release of Luteinizing Hormone (LH) from pituitary gland is the key element in this "concerto" for the stimulation of sex steroid hormones synthesis and the production of mature eggs. Specific alterations in LH pulsatile pattern are linked to hypothalamic dysfunction in female patient with anovulatory infertility - by knowing the information of this pattern, clinicians can decide whether the patient needs treatment with pituitary hormones. However, there is currently no clinical feasible test to assess LH pulsatility due to the need of frequent blood sampling in every 10 minutes for 8 hours, which requires dedicated experts to carry out antibody-based immunoassay and causes significant blood loss to the patient. Here we propose a novel diagnostic strategy by using an electrochemical aptamer-based point-of-care (POC) biosensing system to continuously monitor the LH concentration in the patient with infertility. Our LH aptamer is a single-stranded DNA sequence generated via an *in vitro* selection method which embedded counter-selection steps against FSH and hCG, two structural similar gonadotropins with LH, to avoid cross-reactions. The aptamer can be modified with methylene blue (MB) redox label and coated on the gold surface, which forms a system that can monitor LH-induced structural switching of the aptamer by determining electrochemical currents that are associated with the distance between the redox label and the electrode surface. This system has the potential to be further developed as a POC diagnostic tool for the infertile patient caused by LH defect and assist clinicians to "personalized" treatment with hormonal therapy.