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A *FTH1* gene:pseudogene:microRNA network regulates tumorigenesis in prostate cancer

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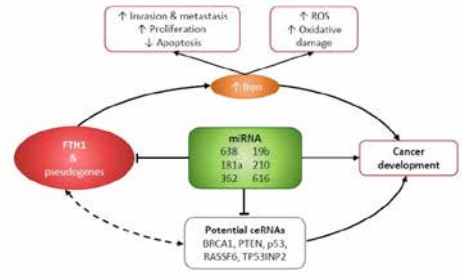
Pseudogenes, non-coding homologs of protein-coding genes, were once considered non-functional evolutional relics. Recent studies have shown that pseudogene transcripts can regulate their parental transcripts by sequestering shared microRNAs, thus acting as competing endogenous RNAs (ceRNAs). In this study, we utilize an unbiased screen to identify the ferritin heavy chain 1 (*FTH1*) transcript and multiple *FTH1* pseudogenes as targets of several oncogenic miRNAs in prostate cancer. We characterize the critical role of this *FTH1* gene: pseudogene: microRNA network in regulating tumorigenesis in prostate cancer, and show that impairing microRNA binding and subsequent ceRNA crosstalk results in complete phenotype rescue. Our results also demonstrate that pseudogenes can regulate intracellular iron levels, which are crucial for multiple physiological and pathophysiological processes. In summary, we describe a novel and extensive gene: pseudogene ceRNA network comprising multiple microRNAs and multiple pseudogenes derived from a single parental gene, which regulates iron storage and tumorigenesis in prostate cancer.



Biography

Yvonne Tay began her research career in Bing Lim's lab at the Genome Institute of Singapore and her PhD work led to key insights into the scope and mechanisms of microRNA activity. Subsequently, she has pursued her Post-doctoral training in Pier Paolo Pandolfi's lab at Harvard Medical School and Beth Israel Deaconess Medical Center under a Special Fellow award from the Leukemia and Lymphoma Society and this research led to the discovery that protein-coding transcripts can co-regulate the tumor suppressor PTEN by competing for shared microRNAs. She has recently returned to Singapore to begin her independent research career. She has been awarded the Singapore National Research Foundation Fellowship and NUS President's Assistant Professorship to continue her research into this previously uncharacterized layer of gene regulation.

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