Evolutionary Insights Into the Stemness Paradox of Human Germ Cells and Cancer Cells

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Primates had evolved an advanced spermatogonia stem cell (SSC) system that correlates with reduced germline mutations and longer lifespans, yet the underlying mechanism remains poorly understood. This study probed the evolutionary underpinnings of stemness maintenance in human SSCs and cancer cells, with a focus on primate-specific cancer-testis-antigen (CTA) genes that have been known to be present in both human testes and cancer cells. Using bioinformatics, I traced the emergence of a panel of human CTA genes that evolved in the ancestor of anthropoids and coincided with the evolution of the advanced SSC system. My experiments involved knockdowns of these CTAs in both human SSCs and cancer cells. The analysis combined both bioinformatics and lab work, with a focus on understanding the functional significance of CTAs in contrasting physiological and pathological contexts. My results revealed that primate-specific CTAs are indispensable for clonal proliferation, a golden standard for high stemness, in both SSCs and cancer cells. Furthermore, my analysis showed that patients with higher level expressions of these CTAs had markedly poorer prognoses and shorter survival times. This research established a direct link among evolutionary biology, human reproductive biology, and cancer biology. It revealed the double-edged nature of CTAs: vital for germline cell maintenance and progeny persistence in humans, yet malignant when hijacked by cancer cells to sustain high stemness in tumors. This dual functionality of CTAs underscores their potential as novel targets for cancer therapy, offering insights into cancer biology and the evolutionary aspects of human physiology.

Awards Won:
First Award of $5,000