Title: Cytokine-driven plasticity in a Prostate Cancer cell line model

Authors:
Thomas Cecchetto[1,2], *Mikael Marttinen*[1,3,4,5], *Antti Kiviaho*[1,3], *Anni Perämäki*[1], *Karishma Sajnani*[1,3], *Barbara Zerbato*[6], *Elina M. Lassila*[1,3], *Sini K. Eerola*[1,3], *Konsta Kukkonen*[1,3], *Hanna Rauhala*[1,3], *Tapio Visakorpi*[1,3,7], *Kirsi J. Rautajoki*[1,3], *Matti Nykter*[1,3], *Alfonso Urbanucci*[1,2,3]

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Abstract

Recent single-cell and spatial transcriptomic studies have revealed a previously unrecognized population of "club-like" secretory cells in the prostate tumour microenvironment (TME). These cells resemble bronchiolar club cells, which serve protective and antimicrobial functions in the lung, but their origin, function, and role in prostate cancer (PCa) remain unclear. They appear near immune infiltrates and sites of inflammation, display stem-like or senescent features, and share traits with normal prostate epithelial cells. Whether they contribute to tumour growth, immune suppression, or reflect inflammation-driven plasticity is unknown.

In this study, we sought to model the emergence of club-like cells in vitro. We exposed LNCaP cells to androgen deprivation and/or acute inflammatory stimuli (TNF-α, IL-1β; 48 h) to induce expression of a club gene signature (PIGR, CP, LTF, SCGB1A1). Expression of androgen receptor (AR) markers was assessed in parallel. Molecular changes were evaluated by RT-qPCR and immunofluorescence (RNA and protein level), while IncuCyte live-cell imaging tracked cytokine tolerability, growth inhibition, cytotoxicity, and morphological dynamics over time.

Our preliminary findings suggest that proinflammatory cytokines induce expression of club-like markers while suppressing AR-regulated genes, consistent with a plastic response to environmental stress.

In the next phase, we will isolate treatment-induced subpopulations by FACS for subculture and functional characterization. Ultimately, we aim to profile the molecular states of club-like cells within the prostate TME using single-cell multi-omics on clinical samples, and to validate in vitro models with the same approaches, with the long-term goal of identifying therapeutic vulnerabilities.