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Squamous epithelia as a paradigm to define the role of stem cells quiescence for longevity

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Adult tissue stem cells maintain tissues throughout life. Therefore, there may be quantitative and qualitative differences in the stem cells of short-lived and long-lived mammals. We hypothesized that one adaptation to longevity could reside within the stem cell compartment, e.g. by enhancing the quality and integrity of the stem cell pool through increased stem cell quiescence and repair. Using squamous epithelia as model systems to explore our stem cell quality-longevity hypothesis, we show that the pattern of proliferation in human oral mucosa fundamentally differs from most other mammals. In contrast to mouse squamous epithelia, proliferation in humans is absent from the basal cell layer and over 90% of proliferating cells are found in the first suprabasal cell layer(s). Therefore, human squamous epithelia have a quiescent basal cell layer that traditionally is viewed as the stem cell layer. The relative proliferative activity of the basal cell layer is correlated with short-livedness in mammals and basal cell quiescence to our knowledge is the only other characteristic that correlates with longevity in addition to body size. Next, we defined the characteristics of this quiescent basal cell layer. Key features in addition to its quiescence are TGF beta expression signatures, polycomb repressor complex 1 (PRC1) expression, expression of a set of well know apoptosis protectors and Hippo signaling components. In a 3D squamous epithelial reconstruct TGF beta signaling was able to induce quiescent basal cell markers supporting a role of this signaling pathway in establishing or maintaining quiescent stem cells in human squamous epithelia.

Biography

Thomas Andl obtained his PhD from the University of Heidelberg, Germany and extended his training in squamous epithelia and hair follicle biology at the University of Pennsylvania and Vanderbilt University. He established mouse models to study BMP, Wnt and microRNA signaling and is interested in how squamous epithelia such as the epidermis or the oral mucosa are maintained under normal conditions and how these epithelia responds to stress, infection and carcinogenesis. His main focus is on the putative stem cells in these tissues and how they are organized, maintained, transformed into cancer and are responding to challenges.

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