In adult tissues there exist a small population of long-lived and relatively undifferentiated cells, which are able to differentiate into all cell types in a given tissue. These, so-called adult stem cells maintain the cellular homeostasis and actively contribute to the repair of the tissue injuries. Because of their longevity, these cells are believed to be the cells of origin for cancers; however, the direct evidence for this is still sparse.

We discovered a new active stem cell population in the mouse hair follicle marked by the expression of orphan G protein-coupled receptor Lgr5. This cell population is initially located at the lower part of the resting hair follicle spanning the lower bulge and the hair germ – structure below the bulge where the growth of a new hair follicle is initiated. Although partly overlapping with the quiescent CD34+ keratinocyte stem cells in the resting hair follicle, the Lgr5-positive keratinocytes actively proliferate during the initiation of the new hair growth and migrate downwards together with the extending hair follicle. When sorted out, the Lgr5 cells display an enhanced colony forming ability when compared to CD34+ cells and were able to form fully developed new hair follicles when transplanted into the nude mice. Lineage tracing experiments confirmed the ability of Lgr5+ cells to form all parts of the growing hair follicle including other identified stem cell compartments (CD34+ and MTS24+ cells).

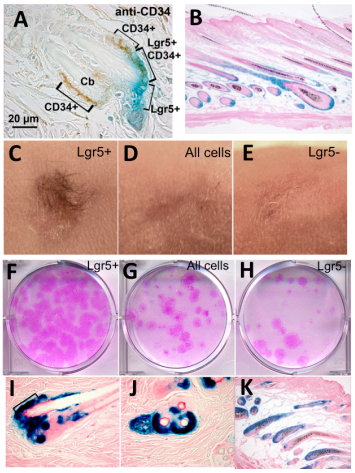

Fig. 1. A-B: Expression of Lgr5 (blue) in resting (A) and growing (B) mouse hair follicles. C-E: Lgr5+ cells reconstitute full-fetaured hair follicles in the transplantation assay. F-H: Lgr5+ cells possess enhanced colony-formation activity. I-K: Lineage tracing of Lgr5+ cells, which reconstitute hair follicle bulge (I, J – cross section) and contribute to all elements of a growing hair follicle (K). Jaks et al. (2008) Nature Genetics.

These observations, together with the results obtained by other groups led to the establishment of a new possible model for the stem cell hierarchy in adult tissues. The active stem cells immediately participate in the normal maintenance of tissue while quiescent cells form an emergency reserve in the case the function or numbers of active stem cells is failing (eg wound healing, irradiation injury). Our work put forward Lgr5 as a new potential adult stem cell marker, which might serve as specific target for drug delivery.

The work described here was published in Nature Genetics, which belongs to the absolute top of the scientific publications and was widely discussed at the scientific forums (annual meeting of the European Hair Research Society as well as in national TV, on the homepage of Karolinska Institute and University of Tartu. Furthermore, the authors received several letters from the general public expressing deep interest in the applicability of the research outcomes in treatment of baldness and skin regeneration.