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## Manipulating the Wnt signaling pathway in mouse intestinal stem cells

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The Wnt signaling pathway plays a crucial role during embryonic development and in adults it participates in stem cell dependent tissue renewal. In order to reveal new aspects of canonical Wnt signaling we generated knock-in mouse with inducible expression of nuclear Wnt inhibitor. In this mouse strain, red fluorescent protein tdTomato is expressed from Rosa26 locus under standard conditions. Upon Cre-mediated recombination its expression is replaced by production of fusion protein EGFP-dominant negative TCF4. Dominant negative TCF4 competes with native Tcf/Lef transcription factors in nucleus and inhibits expression of Wnt target genes. The expression of the fusion protein is lethal during early stages of embryonic development. *In vitro* culturing of so-called organoids originated from intestinal crypts revealed impaired growth of organoids producing dominant negative TCF4 as Wnt signaling is essential for proliferation of the intestinal stem and progenitor cells. Moreover, mouse expressing this protein throughout the intestinal epithelium display disrupted intestinal homeostasis and aberrant proliferation of epithelial cells. Interestingly, induction of dominant negative TCF4 expression in fast dividing Lgr5<sup>+</sup> intestinal stem cells leads to the reduction of this stem cell population but does not affect renewal ability of the epithelium which confirms the assumption of multiple stem intestinal stem cell populations. Eventually, the knock-in mouse strain can be used as a tool for investigation of the role of Wnt signaling in various tissues when crossed to animals expressing Cre recombinase in cell-specific manner.

### Biography

Lucie Tůmová is a Ph.D student shortly before obtaining the degree at the Faculty of Science, Charles University in Prague. She is a member of Laboratory of Cell and Developmental Biology at the Institute of Molecular Genetics of the ASCR, v.v.i. and to the date she has published 6 papers in the international journals.

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