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Does tryptophan metabolism contribute to the escape of cancer stem-like cells from immune surveillance?

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Cancer stem-like cells (CSCs), a recently discovered paradigm of cancer, promote tumor (re-)initiation and maintenance, and provide their resistance to conventional therapeutics. Whether CSCs evolved as progenitor cells that underwent the malignant switch or whether they were 'sculpted' from more differentiated malignant cells by the immune system is not clear. Notwithstanding, CSCs are endowed with properties that help their escape from the immune surveillance. We subjected breast, prostate and mesothelioma CSCs in to expression analysis and compared them to their non-CSC counterparts. Path-way analysis of microarray data revealed that all types of CSCs feature upregulated tryptophan pathway including the *IDO* gene, coding for indolamine-2,3-dioxygenase, the rate-limiting enzyme of the tryptophan pathway causing conversion of Trp to N-formyl-kynurenin. Real-time PCR analysis revealed that the *IDO1* but not *IDO2* isotype was upregulated, and this was confirmed on the protein level. Subsequent analyses were conducted to reveal the mechanism of transcriptional regulation of *IDO* in CSCs and its potential role in the protection of CSCs from the immune system. Since low level of Trp as well as its metabolites prevent activation of effector T cells and promote their apoptosis as well as induction of naïve T cells into T-regulatory cells, we propose that increased Trp metabolism plays an important role in the escape of CSCs from the immune surveillance and their survival in the niche to eventually give rise to second-line tumors. Consequently, targeting Trp metabolism, in particular in combination with inducers of apoptosis, presents a plausible strategy for eliminating CSCs and minimizing tumor recurrence.

Biography

Renata Zobalova is a PhD student at Griffith University, Australia. She has an MSc in Biomedical Science from the same university. Renata Zobalova also holds an adjunct research position at the Institute of Biotechnology, Czech Academy of Sciences in Prague, Czech Republic. She has 11 scientific publications in reputed journals with several as first author as well as a chapter in the book *Cancer Stem Cells*.