CHARACTERISING IMMUNE CELLS IN COLORECTAL TUMORS

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Department: Biomedical Center, Faculty of Medicine in Pilsen, Charles University

Laboratory: Laboratory of Cancer Treatment and Tissue regeneration

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AIM: to assess composition of cytotoxic and immune inhibitory cells in precursor tumors to colorectal cancer (adenomas), in colorectal cancer and adjacent healthy mucosa and lastly in metastases. The results will help to understand the role of various immune cells at different phases of tumor development.

BACKGROUND: Mounting evidence indicates that the immune system plays a key role in protecting against cancer. Animal and human studies demonstrate that, under the pressure of immune surveillance, surviving tumor cells tend to selectively accumulate traits that help them evade immune destruction. A strongly immunogenic tumor in an immunocompetent host may result in optimal stimulation of the immune system and elimination of the tumor. Alternatively, mutated tumor cells selectively develop variants that have acquired insensitivity to immunologic surveillance (e.g., through increased tumor-induced immunosuppression) and that can expand in an unrestrained fashion. A general deterioration of an individual's immune defense may contribute to tumor escape. During first-line anti-tumor immune response, nascent tumors may be detected by lymphocytes of the innate immune system – including natural killer (NK) cells, monocytes, and natural killer T cells – which may lead to the destruction of some tumor cells, uptake and processing of their fragments by macrophages and dendritic cells, and secretion of pro-inflammatory cytokines that attract further immune effector cells to the tumor site. Presentation of tumor-associated antigens to naive CD4+ T helper cells and CD8+ T cells activates adaptive immune response, and activated and antigen-specific cytotoxic T cells expand and home in to the tumor microenvironment, further facilitating tumor cell death. In general,

cytotoxic CD8+ T cells and Th1-type CD4+ T (helper) cells exhibit antitumor activity. By contrast, FOXP3 expressing Tregs and myeloid-derived suppressor cells (MDSC) suppress anti-tumor responses and promote tumor progression and metastasis. Natural killer (NK) cells are sub-classified by their expression of CD56 and/or CD16 cell surface markers, and include cytotoxic and immune inhibitory subtypes. Immune cell types can be identified by immunohistochemistry using markers targeted to specific surface markers of these cells.

METHODS: The present project involves establishment of an immunohistochemical staining battery for the detection of the key immune cell types in pathological slides and frozen tissue samples. The battery will be applied on colorectal cancer related samples, maintained in Pilsen. These include fresh frozen tumor and adjacent mucosal samples, metastatic tumor samples and polyps of early adenomas. The results of cell composition are correlated with clinical and prognostic data.

Qualifications

- Ph.D. (or equivalent) degree in biology or medicine recently graduated
- Technical skills in quantitative histology, organ pathology, immunohistochemistry, experimental work– advanced experience
- High motivation, ability to conduct collaborative research
- Excellent English communication skills both in written and oral form
- Track record of publications in peer-reviewed journals: at least 5 publications in IF journals, two as a first author

The applicants should submit

- Letter of Reference
- Application for post-doc grant at Charles University
- Curriculum vitae
- List of publications
- Copy of university diploma
- Brief description of prior research, skills and experiences