PROJECT SUMMARY

Generation of cross-presenting dendritic cells for immunotherapy in melanoma

In melanoma several tumor-induced mechanisms of immune evasion render the host tolerant to tumor antigens. The maturation of dendritic cells (DC) is suppressed, preventing full T-cell activation and effective antitumor immune response. Cross-presentation is a critical process for the induction of adaptive immunity against melanoma and strategies to enhance this function offer attractive therapeutic targets.

We recently discovered a novel pathway of DC differentiation, finding that, NOD2 activation in antigen presenting cells (APC) induces IL-32 and subsequently cross-presentation. In contrast, GM-CSF derived DC did not efficiently cross-present antigen, but are currently used in cancer immunotherapy. The goal in this proposal is to optimize the generation of cross-presenting DC that are able to elicit a potent anti-tumor $CD8^+$ T-cell response. Immunotherapy in combination with blockade of inhibitory receptors (e.g. CTLA4 or PD1) will be evaluated and can hopefully enhance the antitumor immune response.