Dendritic Cells in Renal Transplant Recipients with Squamous Cell Carcinoma

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Lene Frøyen Sandvik defended her PhD thesis, on September 26, 2013 titled "Squamous cell carcinomas in renal transplant recipients. Analyses of various dendritic cell populations" at the University of Bergen. Opponents and members of the evaluation committee were Liv Eidsmo, Karolinska Institute, Stockholm, Petter Gjersvik, University of Oslo, and Lars Helgeland, University of Bergen. Main supervisor was Silke Appel.

Renal transplant recipients (RTRs) are at high risk to develop cutaneous squamous cell carcinoma (SCC). The aetiology is multifactorial, and reduced immunosurveillance due to long-term immunosuppression is considered to be one of the main risk factors. Dendritic cells (DC) are potent antigen-presenting cells, orchestrate the immune system and play a pivotal role in immunosurveillance. Thus, deficits in DC would impair immunosurveillance and increase the risk of malignancies. Whether RTRs who develop SCC have an altered DC profile compared to RTR without a history of SCC, is unknown. There is a need for increased understanding of the role of DC in RTRs to optimize the management of the patients.

Our aims were to explore whether various DC subsets were altered in long-term immunosuppressed RTR with previous SCC compared to RTR without previous SCC, to explore various DC subsets in SCC of RTRs, and to evaluate the possible use of a vaccination strategy based on monocyte-derived DC (moDC) for the treatment of SCC in RTRs.

The thesis is based on 4 studies. In Paper I and II, various DC subsets were assessed by immunolabelling of peripheral blood and normal skin of RTRs with and without SCC (1, 2). In Paper III, DC subsets were studied by immunolabelling in SCC of RTRs (3). In Paper IV, moDC were generated from blood of RTRs, and phenotype and cytokine/chemokine profile determined by flow cytometry and performance of a 25-plex panel assay, respectively (4).

We found similar numbers of all DC subsets in normal skin and blood of RTRs with and without SCC, indicating that DC quantity cannot be used as a prognostic indicator for development of SCC in long-term immunosuppressed RTRs. We found a reduced number of myeloid DC (mDC) in normal skin and in SCC in RTRs compared to immunocompetent control persons. The reduced number of mDC may contribute to the increased risk of SCC in RTRs and indicates that immunosuppressive medication has an influence on mDC biology. The number of pDC was reduced in blood of RTRs, indicating that immunosuppressive medication also influences pDC. It was possible to generate moDC from RTR in similar numbers as from immunocompetent controls. It was possible to generate moDC from RTR in similar numbers as from immunocompetent controls as a first step towards DC-based immunotherapy.

Lene Frøyen Sandvik defended her PhD thesis. *From left to right*: Tor Hervig (Acting Dean), Petter Gjersvik (Opponent 2), Lene Frøyen Sandvik, Liv Eidsmo (Opponent 1), and Lars Helgeland (member of the evaluation committee). Photo: Karstein Haldorsen.

References

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