

7. Summary

Phenotyping of tumour associated immune cells in equine skin tumours

In this thesis the phenotype of tumor associated immune cells of equine cutaneous skin tumors was examined. Using a wide spectrum of monoclonal antibodies as well as in situ hybridizing and RT-PCR a snapshot of the infiltration pattern of immune cells was taken and possible conclusions were considered.

In the context of this study 200 equine sarcoids, 32 papillomas, 30 melanomas, 29 squamous cell tumors and 27 fibrosarcomas from the files of the Institute for Veterinary Pathology of the Free University of Berlin were rediagnosed using H&E staining. After rediagnosing 179 equine sarcoids, 15 papillomas, 27 melanomas, 25 squamous cell tumors and 19 fibrosarcomas were available for further investigations.

Firstly, these tumors were examined for different tumor associated immune cells by means of immunohistochemical methods. The antibodies directed against human CD3, CD79a, MAC387 (monocytes/macrophages) and S100 showed a positive reaction in equine tissues. Since the MAC387 was positive on both, monocytes and macrophages, equine CD68 was amplified and verified by using RT-PCR and RNA in situ hybridizing (³⁵S-RNA radioactive marked probe). The S100 antibody indicates likewise a wide reaction spectrum, which contains both epidermal Langerhans cells as well as melanocytes and peripheral nerves. For a specific Langerhans cells detection equine CD1a was amplified and verified by RT-PCR in equine skin.

During the process of malignant transformation from "normal" cell to tumor cell, modifications of the cell surface (e.g. expression of tumor antigens, loss of MHC molecules) can occur, which enable a recognition of the tumor cells by the immune system. Humoral and also cellular immune reactions, in which antigen-presenting cells and lymphocytes are involved, lead to the development of specific antibodies and killer cells against the detected tumor antigens. Between the both „effector systems“ of the immune system exist a very complex linkage of specific and nonspecific cooperative regulations. Cell necrosis induced by tumor growth provoke inflammation reactions in the environment. In that process antigen presenting cells

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(APC), for example dendritic cells, play an important role. APC phagocytize tumor cell fragments, present them in processed form to T cells together with MHC molecules or activate natural killer cells directly.

In this work CD68 positive macrophages and T cells were observed as the most frequent cell population in all examined tumors, with exception in fibrosarcomas. This is in agreement with other authors in humans.

In all examined patients potentially cytotoxic effector cells, indicated by the presents of T cells in all tumor, could be observed. These results show an activity of the immune system against that tumors. Despite their potential cytotoxic effects, the T cells observed showed no sufficient tumor control in vivo, since in most cases the tumors did not indicate signs of regressions. Immune cell infiltrates of the examined fibrosarcomas differed from that of other tumors by the fact that lymphocytes played only a subordinated role, while antigen presenting cells were dominating.