9:00 a.m.:

“Mechanism of Lymph Node Metastasis”

Prof. Dotscho Kerjaschki
Medical University, Vienna (Austria)

host: M. Swartz

Abstract:

In individuals with mammary carcinoma, the most relevant prognostic predictor of distant organ metastasis and clinical outcome is the status of axillary lymph node metastasis. Metastases form initially in axillary sentinel lymph nodes and progress via connecting lymphatic vessels into postsentinel lymph nodes. However, the mechanisms of consecutive lymph node colonization are unknown. Through the analysis of human mammary carcinomas and their matching axillary lymph nodes, we show here that intrametastatic lymphatic vessels and bulk tumor cell invasion into these vessels highly correlate with formation of postsentinel metastasis. In an in vitro model of tumor bulk invasion, human mammary carcinoma cells caused circular defects in lymphatic endothelial monolayers. These circular defect were highly reminiscent of defects of the lymphovascular walls at sites of tumor invasion in vivo and were primarily generated by the tumor-derived arachidonic acid metabolite 12SHETE following 15-lipoxygenase-1 (ALOX15) catalysis. Accordingly, pharmacological inhibition and shRNA knockdown of ALOX15 each repressed formation of circular defects in vitro. Importantly, ALOX15 knockdown antagonized formation of lymph node metastasis in xenografted tumors. Furthermore, expression of lipoxygenase in human sentinel lymph node metastases correlated inversely with metastasis-free survival. These results provide evidence that lipoxygenase serves as a mediator of tumor cell invasion into lymphatic vessels and formation of lymph node metastasis in ductal mammary carcinomas.

10:00 a.m.:

“Photodynamic Therapy of Tumors Can Lead to Development of Systemic Antigen-Specific Immune Response”

Pawel Mróz, MD, PhD
Harvard Medical School, Boston, MA (USA)

hosts: H. van den Bergh & P. Nowak-Sliwinska

Abstract:

The mechanism by which the immune system can effectively recognize and destroy tumors is dependent on recognition of tumor antigens. The molecular identity of a number of these antigens has recently been identified and several immunotherapies have explored them as targets. The immune-based therapies act through a mechanism that is distinct from chemotherapy or radiation therapy, and represent a non-cross-resistant treatment. The immune system is capable of recognizing a diverse array of potential tumor antigens. Several proteins, such as CEA, mutated KRAS, mucin-1 (MUC1) and gastrin, have in fact been identified to be specifically overexpressed in most pancreatic cancers and immunotherapies designed to target these antigens have been tested in early-phase clinical trials.

Photodynamic therapy (PDT) is an anti-cancer modality that uses a non-toxic photosensitizer and visible light to produce cytotoxic reactive oxygen species that destroy tumors. PDT has been shown to lead to local destruction of tumors as well as to induction of anti-tumor immune response. The possibility that PDT can elicit specific anti-antigen immunity is clinically significant and should be studied in detail. Our results strongly suggest that certain antigens are important targets for PDT mediated immune response. Understanding the role of antigen-expression in PDT immune response may allow application of PDT in metastatic as well as localized disease.