Institute for Molecular Medicine and Cell Research, University Medical Center, Freiburg

Post-doctoral position on "*In vivo* roles of cathepsin D in breast cancer progression and metastasis in mouse models"

Marie Sklodowska-Curie Individual Fellows programme. A 2-year post-doctoral position will be applied at Marie Sklodowska-Curie Individual Fellowships in 2018 for a French scientist (post-doctoral fellow or PhD student with at least 4 years research experience). The deadline for application is September 2018.

Description – Our research focuses on the *in vivo* functions of cathepsins in different pathologies. The aspartic protease cathepsin D is a poor prognostic marker of breast cancer associated with the metastatic risk. Cath-D is overexpressed by breast cancer cells and abundantly secreted in the breast tumor microenvironment. Cathepsin D stimulates breast cancer cell proliferation, fibroblast outgrowth, angiogenesis, breast tumor growth and metastasis. Whereas clinical and experimental studies established the relevance of cathepsin D in breast cancer, no animal models that provide direct evidence for the role of cathepsin D in tumor formation, progression and metastasis had yet been developed. The aim of this post-doctoral fellow is to evaluate the consequences of increased cathepsin D expression and activity on the behavior of mammary epithelial cells in a newly developed preclinical MMTV-PyMT mouse models so as to mimic the hyper-production of cathepsin D that occurs in so many human breast cancers. Novel transgenic mouse models that overproduce human wild-type cathepsin D or proteolytically-inactive D231N-cathepsin D in their mammary glands invalidated for mouse cath-D had been recently developed in collaboration between T Reinheckel's laboratory (Institute for Molecular Medicine and Cell Research, Freiburg, Germany) and E Liaudet-Coopman's laboratory (IRCM, Montpellier, France). These preclinical mouse models with mammary glands overproducing cathepsin D in an inducible manner will be used to study the cross-talk between epithelial and stromal cells during breast cancer progression and to validate the cathepsin D substrates recently identified. These models will also be useful for testing *in vivo*, the efficacy of the inhibitors of human cathepsin D that are currently being developed.

Host Institution – The Institute for Molecular Medicine and Cell Research aims to a bridge basic life sciences with clinical practice, especially in the area of cancer research. The Institute is integral part of the Freiburg *Comprehensive Cancer Center*, the Cluster of Excellence *Centre of Biological Signaling Studies* and the *Collaborative Research Center 850*. The work of the Reinheckel group is focused on elucidating *in vivo* functions of cysteine and aspartic proteases in mouse models concerning tumor biology, innate immunity, and neurodegeneration.

Candidate –We are looking for a highly motivated candidate with good English communication skills and capacity to work independently in a collaborative

environment ((T Reinheckel's laboratory (Institute for Molecular Medicine and Cell Research, Freiburg, Germany) and E Liaudet-Coopman's laboratory (IRCM, Montpellier, France)). The candidate should have a strong background in cellular and molecular biology. Experience in transgenic mice is also required.

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