Chemisches Kolloquium
Wintersemester 2012/2013

Cathepsin proteases as drug targets for cancer therapy: lessons from transgenic mouse models

PD Dr. Thomas Reinheckel, Institut für Molekulare Medizin und Zellforschung Albert-Ludwigs-Universität Freiburg

Lysosomal cysteine cathepsins belong to a family of 11 human proteolytic enzymes. These enzymes have long been considered to execute the so-called “bulk-proteolysis” inside the lysosome in a redundant manner. When I was about to enter the ‘cathepsin field’ some years ago, my colleagues told: “Well, everything gets chopped down – why are you interested?” Indeed, possible specific functions of individual cathepsins had remained oblivious for the first decades of cathepsin research. Thus in the first part of my presentation I will give a brief introduction into cathepsins and address the key lessons learned from human inherited cathepsin diseases as well as from cathepsin deficient ‘knock-out’ mice.

Expression of some of the cathepsins correlates with progression of a variety of cancers and therefore cathepsins are considered as potential therapeutic targets. However, until recently the contribution of individual cathepsins to tumorigenesis and tumor progression remained unknown. By crossing various types of genetic mouse cancer models with mice in which specific cathepsins have been ablated, our lab contributed to fill this gap of knowledge and I will summarize the results in this presentation. I will further discuss the modes how small molecule inhibitors of cathepsins can be used as cancer therapeutics.