Annual highlights

New core facilities broaden the scope of our research

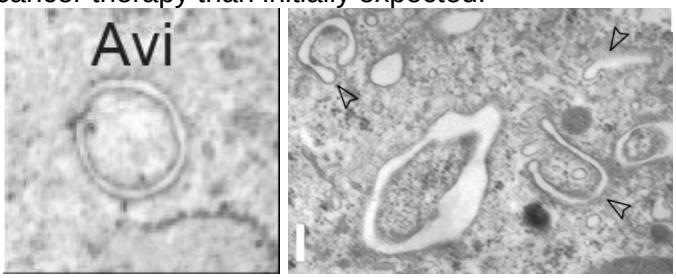
Development and adaptation of new methods are among the major focus areas of the CARD. Accordingly the successful establishment of CARD-initiated lipidomics and bioinformatics core facilities in our Institute scores as the absolute highlight of the year. The lipidomics facility, headed by Dr. Mesut Bilgin, can define the lipid composition of organelles, cells, tissues and body fluids using mass spectrometry-based shot gun lipidomics. The bioinformatics group, headed by Dr. Elena Papaleo, performs multiple important tasks including molecular modelling, data base searches, data analyses and software development. Drs. Bilgin and Papaleo have rapidly integrated to the center and their recruitment has considerably stimulated the cross-disciplinary approaches of our research. Two long-time dreams have come true and I am convinced that these investments will have a major impact on the future success of our center.

Mesut Bilgin, Lipidomics

Elena Papaleo, Bioinformatics

Acid sphingomyelinase is essential for autophagosome closure

Due to our earlier identification of acid sphingomyelinase (ASMase) as an essential enzyme for the maintenance of lysosomal integrity in cancer cells, we have initiated a large research program to develop ASMase inhibitors as anti-cancer drugs that specifically permeabilize lysosomes in cancer cells. In the context of these studies, we found that ASMase activity is also essential for autophagy that normally protects cancer cells against lack of nutrients or oxygen as well as commonly used anti-cancer drugs. Surprisingly, the autophagy defect observed upon ASMase depletion was not due to lysosomal changes. Instead, the accumulating sphingomyelin in ASMase-depleted cells trapped the essential autophagy protein Atg9A in another cellular compartment called recycling endosomes, thereby resulting in the inhibition of Atg9A-dependent maturation and closure of autophagic membranes (Corcelle-Termeau et al, Autophagy in press). Thus, ASMase inhibition may prove to be even more effective strategy for cancer therapy than initially expected.



Transmission electron microscopy images of a normal autophagosome (Avi) in control cells (left) and accumulation of unclosed and swollen autophagic membranes (arrow heads) in ASMase deficient cells (right). Scale bar, 0.2 µm.