**Protein crystallography off the beaten track: Septin filaments, their role in disease and the importance of access to large facilities**

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**1. Introduction**

Septins are GTP-binding proteins which are taken to be the fourth filamentous component of the cytoskeleton and play a fundamental role in cell division. In humans there are 13 different septins, one of which has been recently described to be an off-target substrate for the Zika virus protease. The C-terminal cleavage of septin 2 leads to deficient cell division in neuroprogenitor cells which is believed to be at least partly responsible for microcephaly in new-born infants.

**2. Results**

For the last 15 years we have been attempting to dissect the structure of septins and thereby shed light on their roles in both physiological and pathological processes. Our crystallographic studies have been supported by a plethora of biophysical techniques using research infrastructure from around the world and culminating in the determination of the first 3D structure of a hexameric septin complex solved by cryo-electron microscopy.

The hexamer is one of the basic building blocks of the mature filaments and its structure, together with the isolated C-terminal fragment, has allowed us to rationalize how cleavage by the viral protease affects filament assembly. Our studies have also provided insight into how nucleotide binding and hydrolysis affect filament shrinkage and expansion, how filaments bend and recognize membrane curvature and how cross-bridges are formed during filament bundling. All of the events are important for septin function and will be described in detail during the talk.