Analysis of the cellular functions of *Dictyostelium* strumpellin

Christoph S. Clemen

Institute of Biochemistry I, Medical Faculty, University of Cologne, Cologne, Germany

To date, it is known that mutations of the human VCP gene cause two autosomal-dominantly inherited diseases, inclusion body myopathy associated with Paget disease of bone and frontotemporal dementia (IBMPFD) as well as amyotrophic lateral sclerosis 14, a rare form of ALS. We have identified strumpellin as a novel VCP binding partner. Strumpellin mutations have been reported to cause a pure motor form of hereditary spastic paraplegia (SPG8). We demonstrated that strumpellin is a ubiquitously expressed protein present in cytosolic and endoplasmic reticulum cell fractions. Strumpellin knock-down in human neuroblastoma cells and zebrafish resulted in a significant reduction of axonal outgrowth and lack of motoneuron formation, respectively (Clemen *et al.*, 2010). We now have generated *Dictyostelium discoideum* strains lacking strumpellin or over-expressing GFP- and RFP-tagged wild-type and mutant strumpellin. We will employ these strains for the investigation of the intracellular localization of strumpellin and its cell biological and biochemical functions. We will focus on main cellular processes some of which are known to be affected in hereditary spastic paraplegia, i.e. mitochondrial function, membrane trafficking, proteasomal activity, and autophagy. The use of the model organism *Dictyostelium* will facilitate the analyses of basal cellular functions of strumpellin.