Novel components of Rods and Rings – a subcellular structure with unknown function

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Abstract

The subcellular locations of proteins are closely related to their function and knowledge on subcellular location is important for better understanding of the cellular machinery and characterization of the human proteome. We perform protein profiling on a subcellular level with the aim to determine the subcellular location of all human proteins. We have built a Subcellular Atlas as part of the Human Protein Atlas database[(1,2)]. So far 19000 antibodies have been analyzed with immunofluorescence in human cell lines and the atlas contains subcellular localization data for more than 7000 genes. The acquired high resolution confocal images are manually annotated to one or several of 20 locations such as the large membrane-bound organelles and other well-known subcellular structures. However a fraction of the stainings cannot be placed in any of the known locations and many of these have a fibrous or rod-like appearance.

Here we describe an ongoing effort to characterize the subcellular location of these rod-like immunofluorescent patterns. We found that some of these antibodies target a structure previously described as Rods and Rings, RR. RR is present at a low frequency in human cell lines and a higher frequency in newly thawed cells, rodent cell lines and mESCs. They are observed in the cytoplasm as rods or rings of 2-10 µm or in the nucleus as thinner rods. There are only two known components of RR, Inosine monophosphate dehydrogenase (IMPDH2) and Cytidine triphosphate synthetase (CTPS1), both rate-limiting enzymes in biosynthesis of GTP/CTP. Formation of RR can be induced in all cells by inhibition of one of these two enzymes and it has been speculated that these enzymes cluster together as a response to decreased intracellular levels of GTP/CTP. We have now identified an additional 20 proteins believed to be components of RR and the networks around these proteins are now being investigated.

(1) Barbe et al (2008) “Toward a confocal subcellular atlas of the human proteome”, Mol Cell Proteomics 7(3):499-508.
(2) Uhlén et al (2010) ”Towards a knowledge-based human protein atlas”, Nat Biotechnol 28(12):1248-50.