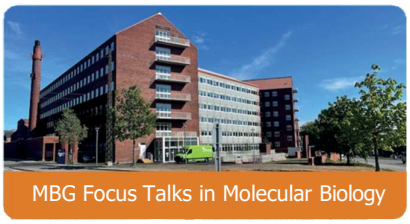
# MBG FOCUS TALK

Hosted by Daan van Aalten




**Monday 16 September 2024 @ 10:00-10:45**
Faculty Club (1870-816)


## Alex Faesen

**Max Planck Research Group Leader**

**Biochemistry of Signal Dynamics**

**Max Planck Institute for Multidisciplinary Sciences**

**Göttingen, DE**


## Protein metamorphosis as responsive signalling node

Metamorphic proteins can switch between distinct native folds under physiological conditions. The last few years, our biochemical reconstitutions have shown that regulated metamorphosis controls the assembly (and disassembly) of key signalling- and effector-complexes in space and time. The emerging paradigm is that the metamorphic HORMA domain proteins default to an inactive state, before converting to a partner-bound active state. Since metamorphosis is typically slow, this creates a rate-limiting step in signalling or the assembly (and disassembly) of effector complexes.

Crucially, metamorphosis can be accelerated by specialized protein machines, thereby creating a regulated rate-limiting step in signalling. For example, the Spindle Assembly Checkpoint (SAC) crucially delays mitosis in metaphase until all chromosomes are bi-oriented. Our reconstitution of a near-complete SAC signalling network elucidated how the catalysed metamorphosis of MAD2 creates the essential regulatory complex. The core properties in MAD2-based signalling are likely conserved in other HORMA domains proteins. In our most recent work, we explored how REV7, ATG13 and ATG101 use their metamorphosis to regulate the assembly of signalling complexes in DNA damage repair and autophagy. I'll also present our reconstitution of the membrane contact site that is responsible for the initiation of human autophagy, which identified ATG13 and ATG101 as metamorphic regulators of its assembly and function.

AARHUS UNIVERSITY