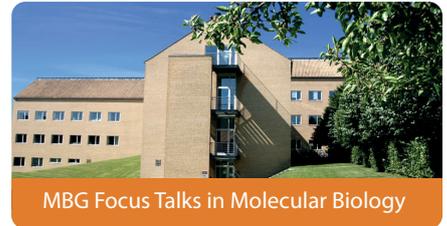


# MBG FOCUS TALK

hosted by Gregers Rom Andersen, Section for Structural Biology



**Friday 29-3-2019 11:00**

Science Park Building 3140-114 Meeting room 5

**Prof Hans Bakker**

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## Functional aspects of C-mannosylation

C-mannosylation is a form of protein glycosylation in which single mannose residues are covalently attached to tryptophans in a unique C-C linkage. *C. elegans* DPY-19 was the first identified C-mannosyltransferase (1). Dpy-19 mutants have a characteristic dumpy phenotype. With increasing temperatures, the phenotype was shown to become more severe and finally lethal. This suggested that target proteins of the C-mannosyltransferase are increasingly dependent on their glycosylation state at rising temperatures.

C-mannose is found on many different proteins, but is characteristic for thrombospondin repeats, which are found in various numbers in about 100 proteins. The mannose attached to tryptophans in a consensus WxxWxxWxxC sequence are involved in a tryptophan-arginine ladder that forms the core of the repeat. There are at least two different C-mannosyltransferases in mammals that act on different tryptophans of this motif (2).

We are able to produce target proteins with and without C-mannose in mammalian cells and *Drosophila* S2 cells and thus can study the function of C-mannosylation for different proteins. We could show that secretion of TSR domains of *C. elegans* UNC-5 increased with C-mannosylation. Secretion of non-mannosylated domains was highly impaired with increased temperature, reflecting the *C. elegans* dpy-19 phenotype and suggesting C-mannosylation to influence protein stability. Thermal denaturation experiments monitored using circular dichroism spectroscopy confirmed the stabilizing effect of C-mannose. Denaturation of the TSR domain under reducing conditions and refolding experiments showed that C-mannose has a positive effect on folding. Molecular dynamics simulations supported the experimental data.

1. Buettner F. F. R., Ashikov A., Tiemann B., Lehle L., Bakker H. (2013) *C. elegans* DPY-19 is a C-mannosyltransferase glycosylating thrombospondin repeats. *Mol Cell*, 50:295-302