

Postdoc position available at the Sibon lab. (University Medical Center Groningen, The Netherlands) for the following project on the intersection between chemistry and cell biology.

Coenzyme A is an essential metabolic cofactor for living organisms and is mostly known for its role in over 100 cellular metabolic reactions. We and others demonstrated that Coenzyme A is also a key factor in protein modifications and signal transduction, further expanding the prominence of Coenzyme A in living organisms.

Until very recently, the consensus has been that intracellular Coenzyme A is obtained exclusively by a universally conserved five-step, *de novo* biosynthesis pathway in the cytosol of each cell, which begins with the uptake of vitamin B5. Patients with an inborn-error of this pathway suffer from neurodegeneration. Recently, we have demonstrated that cells and organisms have an alternative strategy for obtaining Coenzyme A, which involves the uptake of extracellular Coenzyme A. In particular, we have shown that various eukaryotic cells and organisms convert Coenzyme A present in the environment extracellularly into 4'-phosphopantetheine. This metabolite is subsequently incorporated into cells and converted back into Coenzyme A. This project is aimed to investigate the physiological relevance of this discovery.

Preliminary results using validated fruit fly models suggest a possible flow of Coenzyme A (precursors) between organisms, namely from mothers to progeny or from microflora to the host.

By using these models and newly developed sensitive analytical detection methods for Coenzyme A and its precursors, the project aims to provide proof for intra-organismal flows of Coenzyme A. This research will change longstanding Coenzyme A concepts with possible impact on health and disease, especially for the treatment of inborn-errors of Coenzyme A biosynthesis.

See also:

<http://cellbiology.umcg.nl/>

1) Sibon O.C.M. & Strauss E. Coenzyme A; to make it or uptake it. **Nat Rev Mol Cell Biol** 17, 605-606 (2016)

2) Srinivasan B, Baratashvili M, Hayflick S, Colombelli C, Van der Zwaag M, Kanon B, Schaap O, Nollen E, Tiranti V, Podgoršek A, Kosec G, Petković H, Reijngoud D.J., Grzeschik N.A, Sibon O.C.M. Extracellular 4'-Phosphopantetheine is a stable and novel substrate for intracellular Coenzyme A synthesis. **Nature Chemical Biology** 2015 Oct;11(10):784-92)

Position for 1 year with an extension of another 2 years.

Candidates must have obtained their PhD and must have a strong publication record. A background in chemistry is preferable but not a requirement.

Ody Sibon: o.c.m.sibon@umcg.nl