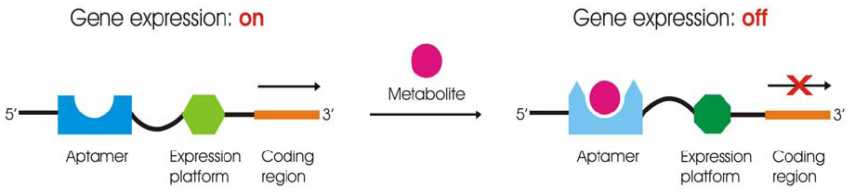
Master project:

Investigations on the interaction between new B_{12} peptide derivatives and the *btuB* riboswitch

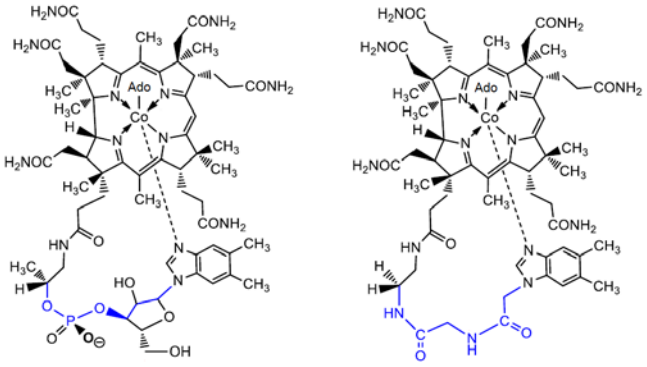
Advisors: Prof. Roland K. O. Sigel, PD Dr. Felix Zelder
Supervisors: Anastasia Musiari, Marjorie Sonnay

General: Riboswitches are small conserved RNA sequences involved in the control of gene expression through the binding to specific metabolites.[1] Upon binding, this special RNA-sequences "switch" their structure and block the transcription and/or translation. Since riboswitches are mostly found in bacteria, they are an ideal target for antimicrobial drugs. A deep understanding of the metabolite-riboswitch interaction could help in the design of structural analogues of the natural metabolite to block riboswitches of pathogens and to interfere with their gene expression.
The focus of our research lies in the binding mechanism between the *btuB* riboswitch of *E. coli* and its natural ligand, coenzyme B_{12}. Past studies[2,3] led to the question which are the structural requirements on the complex B_{12}-metabolite to bind and switch this RNA.
Chemical modifications on different functional sites of the B_{12}-molecule can be performed in order to elucidate the importance of the different moieties for the structural rearrangements of the riboswitch.



General scheme of gene regulation by B_{12}-riboswitches

Task of the project: The project is divided in two parts, the first supervised by Marjorie Sonnay (Zelder group) and the second by Anastasia Musiari (Sigel group). The first period focuses on the synthesis of B_{12} derivatives modified on the lower loop by replacing the sugar phosphate with a peptide backbone (B_{12}-peptides).[4] The apical CN- substituent will be then substituted with an adenosine moiety to get the correspondent coenzyme analogues.[5]
The second period focuses on the interaction between the RNA and the new synthesized B_{12} derivatives. The main biochemical technique used will be in-line probing.[6] To perform these experiments ^{32}P-5'-labeled RNA will be synthesized. All steps involving radioactive materials will be held in the ^{32}P-radiolab of the Department of Chemistry.



Coenzyme B_{12} VS. a prototype of Peptide B_{12}

Your profile: You should be a chemist or a biochemist with a strong interest in both synthetic chemistry and biochemical techniques.

Remarks: The project will be supervised in English and will be held at the Department of Chemistry of the University of Zurich (Winterthurerstrasse 190, CH-8057 Zürich)
Additional information about the project can be obtained by contacting Anastasia Musiari (anastasia.musiari@chem.uzh.ch) or Marjorie Sonnay (marjorie.sonnay@chem.uzh.ch).

[1] R. R. Breaker, *Mol. Cell* **2011**, *43*, 915.
[2] S. Gallo, M. Oberhuber, R. K. O. Sigel, B. Kräutler, *ChemBioChem* **2008**, *9*, 1408.
[3] S. Gallo, S. Mundwiler, R. Alberto, R. K. O. Sigel, *Chem. Commun.* **2011**, *47*, 403.
[4] F. Zelder, K. Zhou, M. Sonnay, *Dalton Trans.* **2013**, *42*, 854.
[5] K. L. Brown, S. Cheng, H.M. Marques, *Polyhedron* **1998**, *17*, 2213.
[6] E. E. Regulski, R. R. Breaker, *Methods Mol. Biol.* **2008**, *419*, 53.