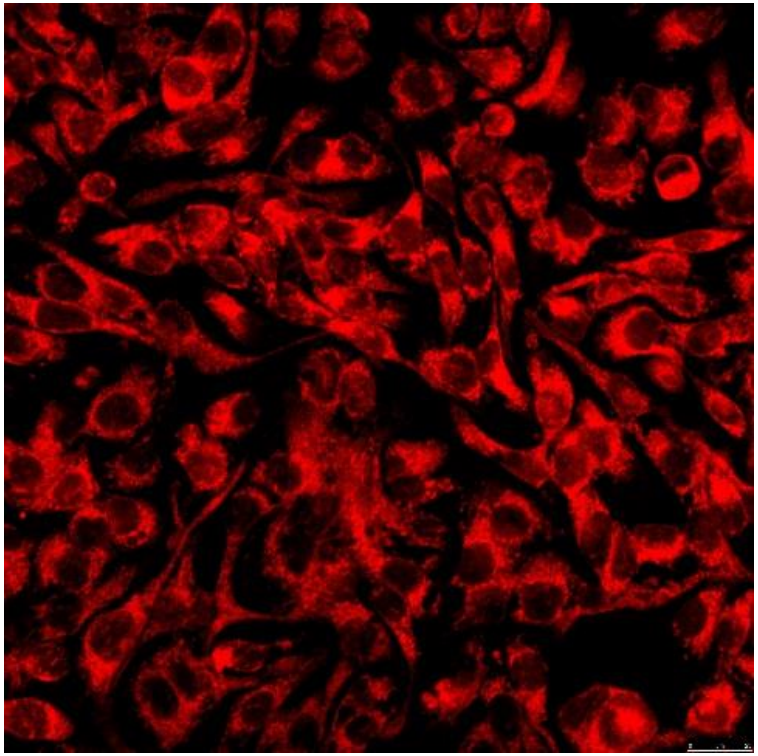
Theracat



Gerard Roelfes

Stratingh Institute for Chemistry

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http://www.roelfesgroup.nl

Stratingh Institute for Chemistry

The mission of the Stratingh Institute for Chemistry is to perform excellent research and teaching in molecular and supramolecular chemistry.

Core activities in the chemical sciences such as bioorganic chemistry, organic chemistry, molecular inorganic chemistry and molecular materials chemistry are embedded in the institute. The research programme is focussed on synthesis, catalysis, functional materials, bio-organic chemistry/chemical biology and systems chemistry/complex molecular systems.

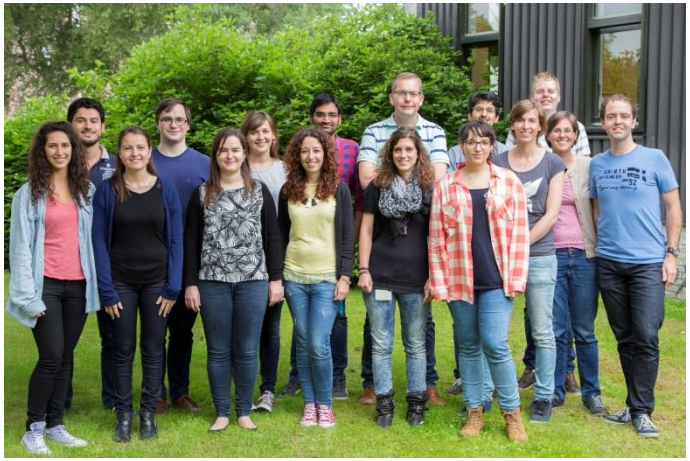
14 research groups

Roelfes Group

Interface Chemistry/Biology, with a focus on bioinspired catalysis

Topics:

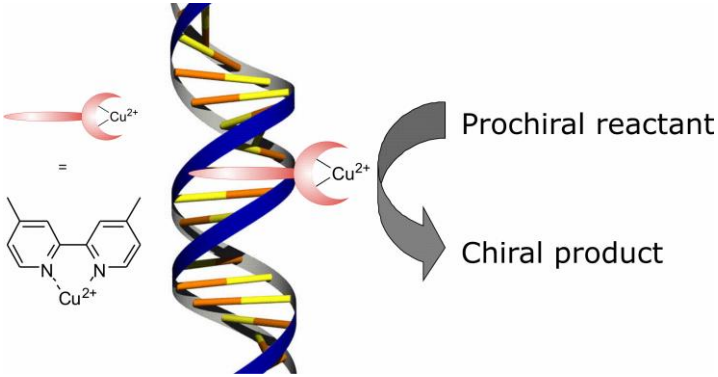
- *Design of (artificial) enzymes*
- *Bio-orthogonal catalysis*
- *Catalytic chemistry in living cells*

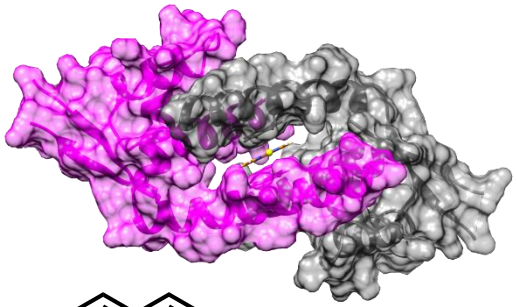


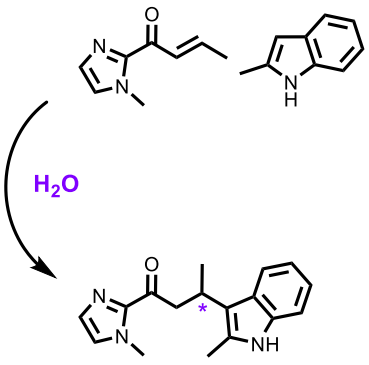
Current composition:
1 PI, 7 PhD students,
4 postdocs, 3 MSc students

Research in the Roelfes group

Artificial enzymes / enzyme design

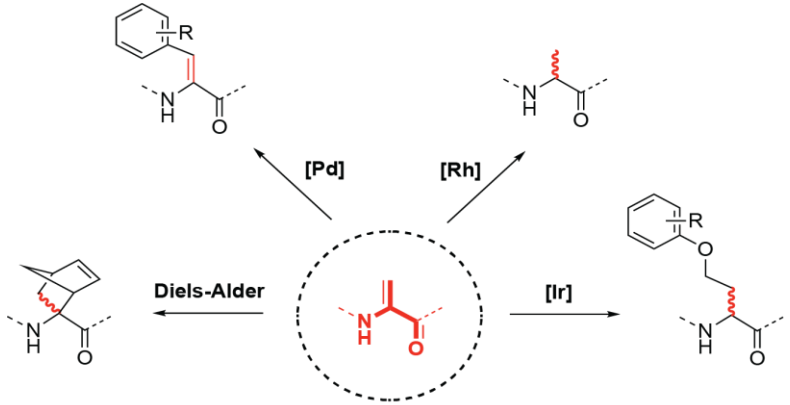






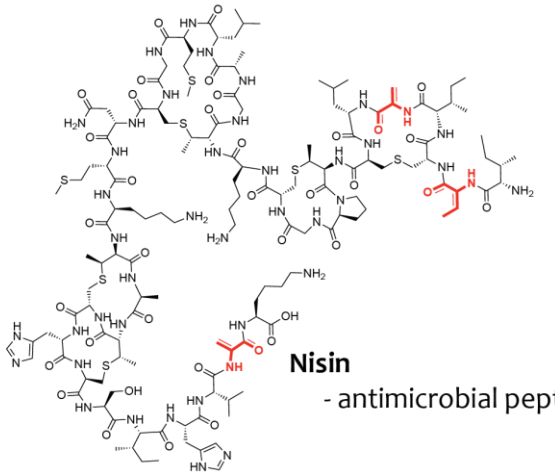
Friedel - Crafts

Bioorthogonal catalysis



dehydroalanine

- natural amino acid
- unnatural catalysts for specific modification

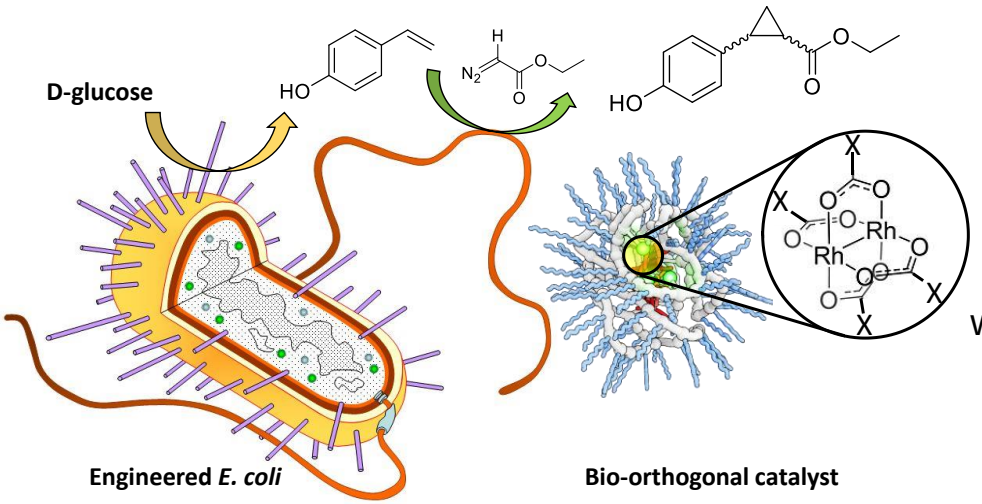


Nisin

- antimicrobial peptide

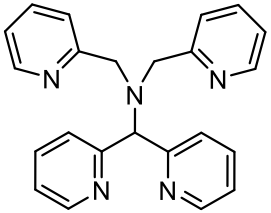
Catalysis in (combination with) Living Cells

A hybrid metabolism:

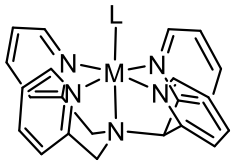


with Anja Palmans (TUE)

Catalysis in (combination with) Living Cells



N4Py

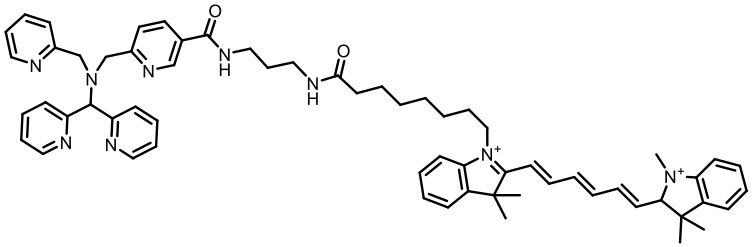


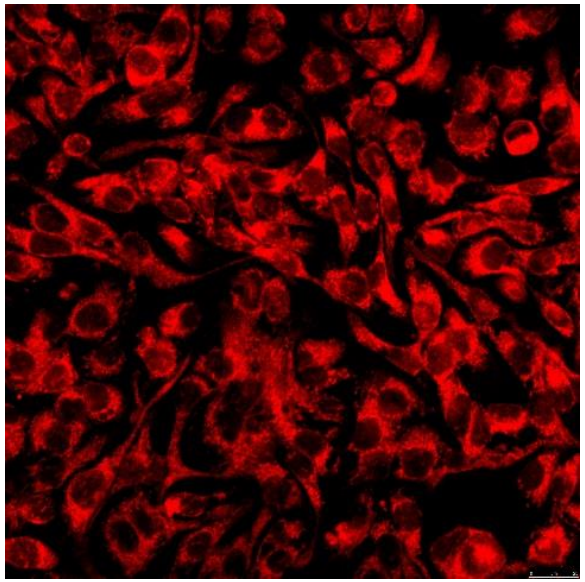
Metal-N4Py complex

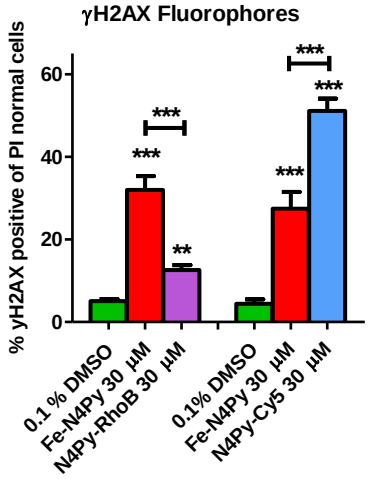
M = Fe(II), Cu(II), Mn(II), Zn(II) ; L = CH_3CN

M = Fe(III) ; L = CH_3O^-

Fe-N4Py produces hROS in cells

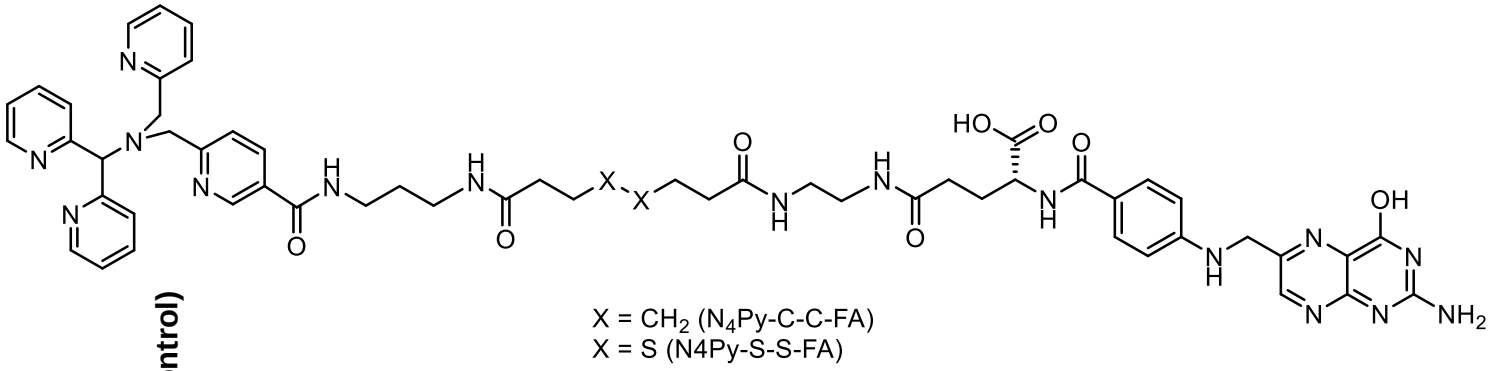




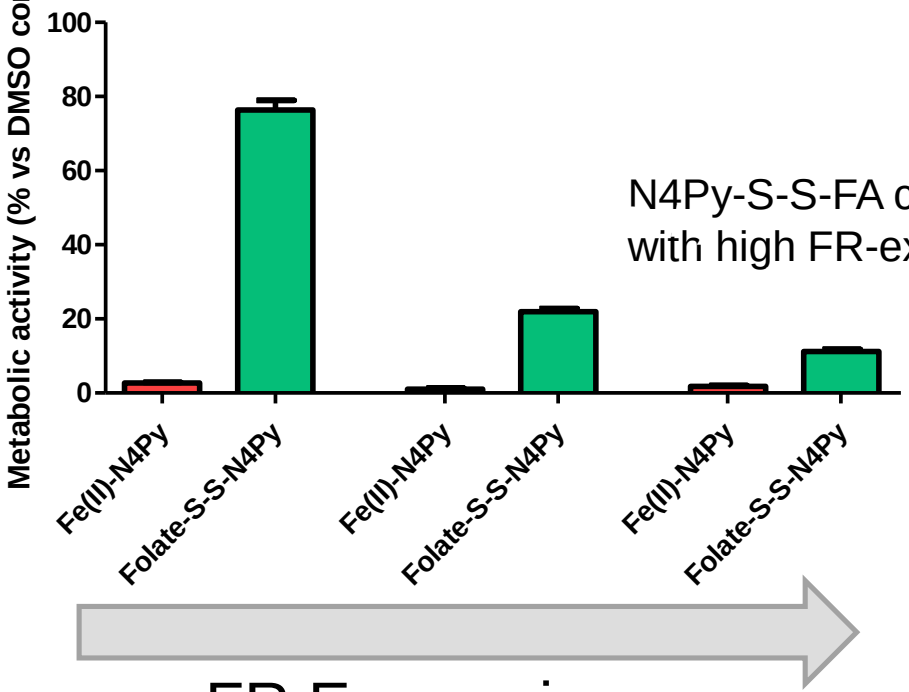


With M.G. Rots (University Medical Center Groningen);
ACS Chem. Biol. 2014, 9, 1044;
Inorg. Chem. 2018, under revision;
In preparation.

Selective Targeting of Cancer Cells



X = CH_2 (N_4Py-C-C-FA)
X = S (N4Py-S-S-FA)



N4Py-S-S-FA conjugate towards cells with high FR-expression

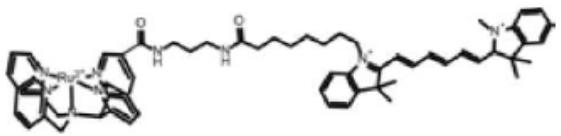
FR Expression

Roelfes group in Theracat

ESR 1 - GRO	Novel Ru and Pd Complexes of Polypyridine for Catalysis in Living Cells	PhD: Yes	Deliv.: 3.1, 5.1	Start date: M6	Duration 36	WP3

Objectives: **1.** Development of Ru and Pd complexes for catalytic uncaging of prodrugs in cancer cells; **2.** Synthesis of targeted metal complexes by conjugation to targeting moieties; **3.** Development of light activable Ru complexes for spatial and temporal control over catalytic uncaging of prodrugs.

Description: In this project, we aim to develop Ru(II) and Pd(II) complexes of polypyridine ligands for catalytic uncaging of anti-tumour drugs in cancer cells. Metal complexes of polyridyl ligands such as phenanthroline, terpyridine, TPA and N4Py are of interest because of their broad catalytic scope and, as recently shown in our group, are efficiently taken up by cancer cells. Moreover, targeting to specific cellular location can be achieved by conjugation to hydrophobic dyes targeting, for example, the mitochondria. We will prepare a variety of Ru(II) and Pd(II) complexes and investigate them in uncaging of prodrugs, first in model reactions and then in vitro. When required, the complexes will be incorporated in delivery vehicles such as single chain polymer nanoparticles, micelles and lipidic nanoparticles developed in WP3. Finally, light activable variants of active Ru(II) complexes will be prepared and tested by ligation of nitrile ligands to the open coordination sites, which can be dissociated by light irradiation.



Planned secondments: EDI – Prodrug uncaging in vitro (M12, 3 months); **TEVA** – Formulation (M24, 3 months).	**Expected results (deliverables)**: Pd and Ru complexes for catalytic uncaging of prodrugs (D3.1); specific targeting of complexes to cellular location (D5.1); light activable Ru complexes for uncaging of prodrugs (D3.1)