Natural products as probes in pharmaceutical research: Nannocystin A, an inhibitor of the elongation factor 1a

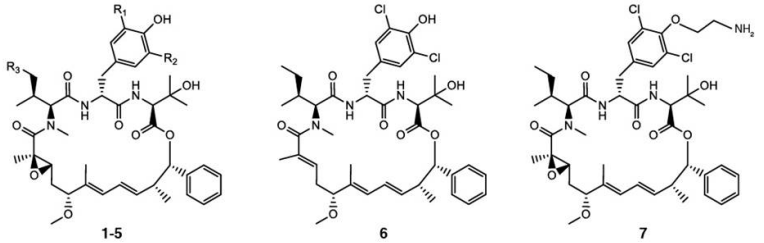
P. Krastel[1], E. Schmitt[1], D. Hoepfner[1], M. Schierle[2], S. Roggo[1]

[1]Novartis Institutes for Biomedical Research, Basel, Switzerland, [2]Novartis Institutes for Biomedical Research, Cambridge, US

From the start of the pharmaceutical research natural products played a key role in drug discovery and development. Over time many discoveries of fundamental new biology were triggered by the unique biological activity of natural products. Unprecedented chemical structures, novel chemotypes, often pave the way to investigate new biology and to explore new pathways and targets [1].

The cyclic lactone Nannocystin A, obtained from the cultivation of myxobacteria from the Nannocystis genus, displayed in biological assays antifungal and cytotoxic activities. Combined genetic and proteomic approaches identified the eukaryotic translation elongation factor 1a (EF-1a) as the target of this compound class [2].

The talk will focus on the discovery of this compound class and will guide trough the target identification of this compound class.



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Cpd No.	Name	R_1	R_2	R_3	HCT116 IC_{50} (nM)
1	Nannocystin A	Cl	Cl	Me	2.6
2	Nannocystin A1	H	Cl	Me	5.3
3	Nanncystin A0	H	H	Me	3.7
4	Nannocystin B	Cl	Cl	H	7.2
5	Nannocystin B1	H	Cl	H	2.8
6	Nannocystin Ax		see above		5.4
7	Derivative		see above		7.1

[1] E. Schmitt, D. Hopefner, P. Krastel (**2016**), Natural products as probes in pharmaceutical research. *Journal of Industrial Microbiology & Biotechnology 43*, 1691-1699.
[2] P. Krastel, S. Roggo, M. Schirle, N. Ross, F. Perruccio, P. Aspesi, T. Aust, K. Buntin, D. Estoppey, B. Liechty, F. Mapa, K. Memmert, H. Miller, X. Pan, R. Riedl, C. Thibaut, J. Thomas, T. Wagner, E. Weber, X. Xie, E. Schmitt, D. Hoepfner (**2015**), Nannocystin A: an elongation factor 1 inhibitor from myxobacteria with differential anticancer properties. *Angewandte Chemie International Edition* 54, 10149-10154.