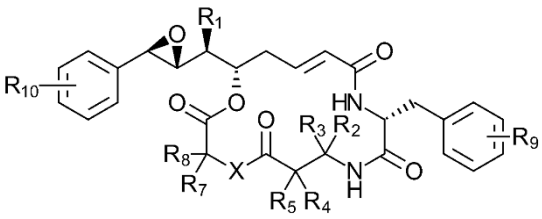
New Cryptophycins for ADC and SMDC

New conjugation of cryptophycins for use in ADC (antibody-drug conjugates) and SMDC (small molecule drug conjugates)

Invention

Cryptophycins are discussed as potential medicaments against cancer due to their high cytotoxic and cytostatic effect. They target tubulin and block the microtubule formation, leading to high cytotoxicity against many cancer cell lines. Moreover, as they are a weak target for the P-gp efflux pump, the cytotoxicity is only slightly reduced in multidrug-resistant (MDR) cancer cells. Due to these characteristics, several cryptophycin analogues were investigated as chemotherapeutics and cryptophycin-52 was even brought to the clinics. However, these were discontinued in phase II because of neurotoxic side effects and insufficient efficacy. These effects made a direct approach unusable for cancer treatment so far.



General formula of cryptophycin compound

To circumvent such side effects, cryptophycin could be used as payload for drug-conjugates. For treatment of solid tumours ADCs have only little effects, therefore SMDCs have more advantages in relation. To date, there are only few ADCs approved for cancer therapy and higher diversity is desirable to compensate for emerging resistances. In addition, there is also need in the art for novel, highly potent toxins, with no cryptophycin-based ADCs being approved so far.

The present invention combines new synthetic ways to new Cryptophycin derivatives with alternative conjugation possibilites and pico-molar cytotoxicies, for ADC and SMDC synthesis. It can be linked to selective antibodies, peptides or other ligands which address tumour antigens and may therefore be used for anticancer therapy.

Commercial Opportunities

The present invention allows for new strategies in the semisynthetic synthesis of ADCs and SMDCs for treatment of cancer. On behalf of University of Bielefeld, PROvendis offers a patent license as well as a research collaboration with licensing option to innovative companies.

Current Status

In case of interest, we will be pleased to inform you about the patent status.

Relevant Publications

Anselmi M, Borbély A, Figueras E, Michalek C, Kemker I, Gentilucci L, Sewald N.; “Linker Hydrophilicity Modulates the Anticancer Activity of RGD-Cryptophycin Conjugates.”; Chemistry. 2021, 27(3),1015-1022

Borbély A, Thoreau F, Figueras E, Kadri M, Coll JL, Boturyn D, Sewald N.; “Synthesis and Biological Characterization of Monomeric and Tetrameric RGD-Cryptophycin Conjugates.“; Chemistry. 2020, 26(12), 2602-2605

An invention of Bielefeld University.

Competitive Advantages

- High potent cytostatic and cytotoxic effect
- Less side effects
- Novel access via conjugation in alternative position
- Higher yields in synthesis
- New cryptophycin payloads

Technology Readiness Level

1 2 3 4 5 6 7 8 9

Technology validated in lab

Industries

- Biotechnology Industry
- Pharmaceutical Industry

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