New bifunctional Prodrugs with cleavable linker for targeted tumor therapy (ADC)

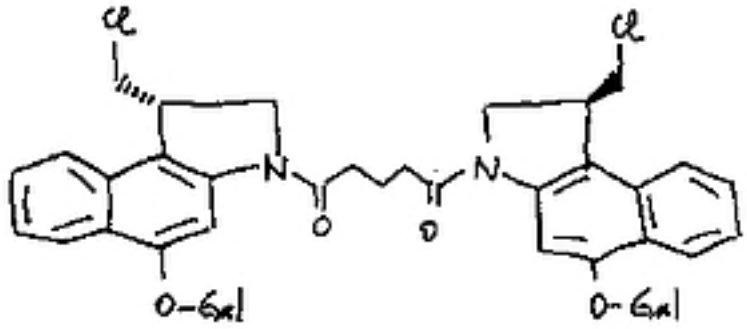
Antibody tumor therapies have provided therapeutic benefit to patients with cancer, autoimmune diseases and other serious medical conditions. However, many antibodies lack sufficient intrinsic anti-tumor activity to be used as first-line therapeutics. Scientists at the University of Göttingen developed new and highly potent drugs with cleavable chemical linkers to develop tumor specific antibodies for selective and highly effective tumor therapy (ADC).

Challenge

Selective tumor therapy combines the benefits from classical chemotherapy and antibody tumor therapy by providing antibody-drug-conjugates (ADC). These conjugates must provide safe medical application (prodrugs) and extremely high toxicity within the targeted tumor cell (activated drug). Thus, there is a high medical unmet need to provide ADCs with stable but cleavable chemical linker to safely and effectively release highly toxic payloads.

Our Solution

Scientists at the University of Göttingen developed new and highly potent prodrugs/drugs with cleavable chemical linkers for ADCs. The soluble prodrugs are activated into highly cytotoxic drugs (IC_{50} in the pico-molar range) only in targeted tumor cells.

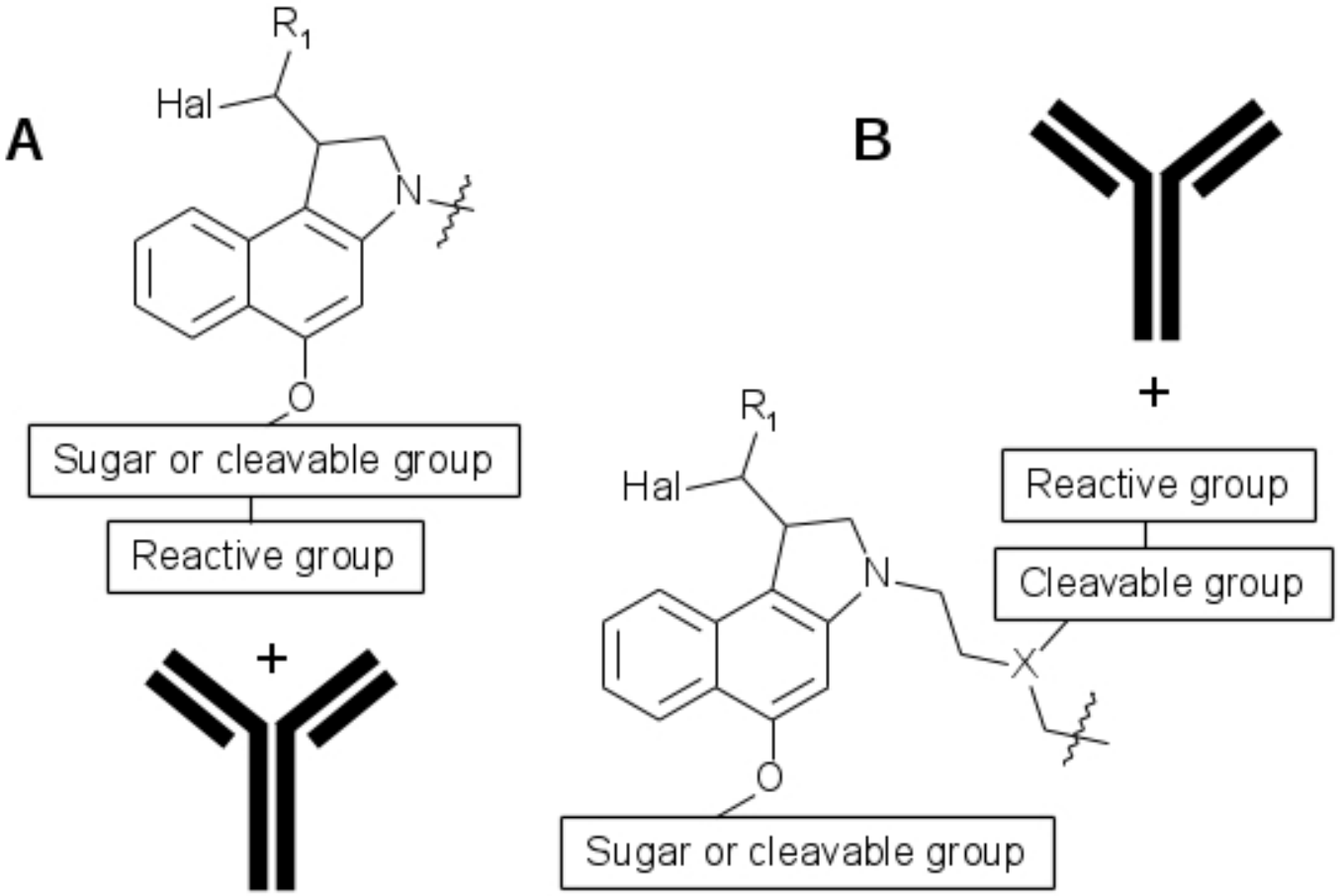


Our 2nd generation bifuncional prodrug with two CBI alkylation units (CBI = cyclopropabenzindole).

MBM Science Bridge GmbH
Hans-Adolf-Krebs-Weg 1
37077 Göttingen / Germany
www.sciencebridge.de

Advantages

- New chemical linker design based on our 2nd generation bifunctional prodrugs/drugs (Duocarmycin origin).
- Different linker designs to allow for alternative antibody-coupling - even dual coupling possible.
- Prodrug has low cytotoxicity, whereas drug is highly totoxic in low pico-molar range.
- Chemical linker with cleavable group for release and activation of prodrug into drug inside targeted tumor cell.
- Expected improvement in safety through bigger therapeutic window (QIC_{50} Prodrug/Drug = 1.000.000).
- Specific and effective chemical coupling to antibodies.
- Payload with new MoA: highly toxic non-DNA binding alkylating agent.



MBM Science Bridge GmbH
Hans-Adolf-Krebs-Weg 1
37077 Göttingen / Germany
www.sciencebridge.de

New chemical linker design to antibodies based on our 2nd generation bifuncional prodrugs/drugs. A) Linkage via CBI alkylation unit. Since there are two CBI units in the full molecule, linkage of two antibodies are possible. B) Linkage via CBI linker unit.

Applications

ADC Tumor Therapy.

Developmental Status

In vitro tested prodrugs/drugs having cleavable linker for direct antibody coupling.

Patent Status

An international patent application has been filed and a new patent application (improvement) will be filed. (WO2017072295A1, Applicant: Georg-August-University of Göttingen public law foundation).

DE102009051799A1 (2nd generation bifunctional prodrugs/drugs (Duocarmycin origin).

References

- Tietze et al. Angew. Chem. Int. Ed. 2010, 49(40), 7336-9.
- Wirth et al. Angew. Chem. Int. Ed. 2012, 51(12), 2874-7.
- Wirth et al. Angew. Chem. Int. Ed. 2013, 125(27), 7059-63.
- Chen et al. Mol Pharm. 2013 May 6;10(5):1773-82.
- Koch et al. Angew. Chem. Int. Ed. 2015, 54(46), 13550-4.
- WO2017072295A1.
- DE102009051799A1 (2nd generation bifunctional prodrugs/drugs (Duocarmycin origin).

Contact

Dr. Stefan Uhle
Patent Manager Life Science
E-Mail: suhle(at)sciencebridge.de
Tel: +49 551 30724 154

Reference: BioC-1848-SUG

MBM Science Bridge GmbH
Hans-Adolf-Krebs-Weg 1
37077 Göttingen / Germany
www.sciencebridge.de