Synthetic Antibodies against Cyclodepsipeptide Toxins

Background:

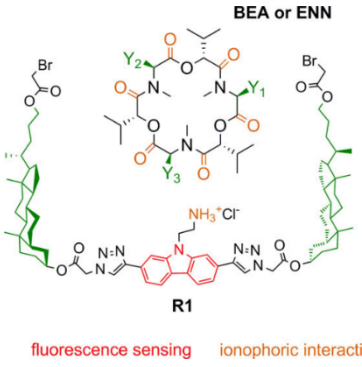
Beauvericin (BEA), Enniatins (ENN) & Cereulide (CER), are toxic cyclodepsipeptides (CDPs) that contaminate many food products. CER is produced by *Bacillus cereus* and causes acute toxic symptoms. It is found in a variety of food products incl. rice, pasta, noodles, and dairy products. BEA and ENN are produced by *Fusarium* and thus present in many grain-based food products. They represent a chronic health risk.

Challenge:

To mitigate these health risks, high-throughput detection and quantification methods for these CDP toxins and/or pre-treatment methods for contaminated food are required. Today, Today, CDPs can only be analyzed via LC-MS – an expensive, low-throughput method. BEA, ENN & CER are non-immunogenic (too small, hydrophobic). Therefore, the development of specific antibodies is not possible.

Technology/results:

Ghent University developed a large collection of artificial receptors (synthetic antibodies or SynABs) that specifically bind CDPs. To date, SynABs are the only technology with high-throughput potential to bind and quantify CDPs. Highly specific SynABs against BEA & ENN (Ornelis et al., 2019; see figures 1 & 2) as well as CER (unpublished data) have been developed.



	Y_1	Y_2	Y_3
BEA	Bn	Bn	Bn
ENN A	sBu	sBu	sBu
ENN A1	sBu	sBu	iPr
ENN B	iPr	iPr	iPr
ENN B1	iPr	iPr	sBu

Fig 1: Structure of SynAB R1 with color-coded indication of the interactions with BEA (K_{BEA} = 4.0 x 10^5 M^{-1}) and the most common ENN subtypes.

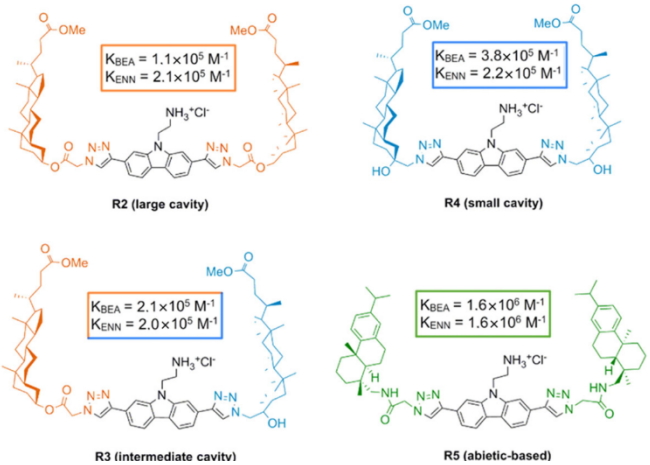


Fig 2: Structures & binding affinities of SynABs R2 - R5 for BEA & ENN (K_{BEA} & K_{ENN}).

In a proof-of-concept study, a markedly reduced cytotoxicity of CDPs was demonstrated when human cell lines were treated with specific SynABs (Ornelis et al., 2019; see figure 3).

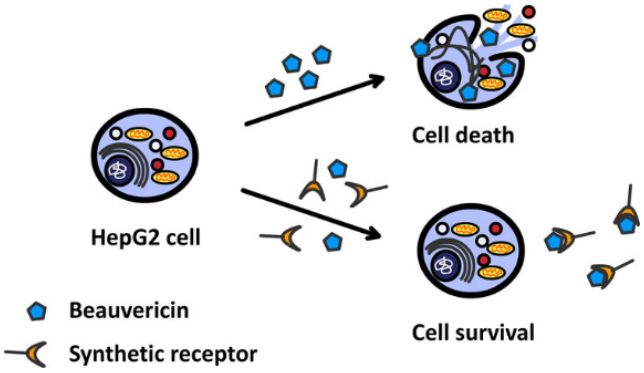


Fig 3: Use of SynABs to prevent CDP-mediated cell death.

In addition, solid-phase extraction methods have been established with the potential to remove CDPs from food products (unpublished data).

Chemical synthesis protocols for the most promising SynAB's have been established (Ornelis et al., 2018 & 2019, and unpublished data).

Application fields:

- High-throughput analytics of CDPs (CER, BEA & ENN) in food samples;
- Pre-treatment & removal of CDP toxins from food products;

Opportunity:

Licensing opportunity for patent family "Synthetic receptors for ionophoric compounds" (WO 2019/166475 A1), granted in the US & Australia (US11608326B2, AU2019228686B2); pending in Europe & Canada (EP3759099A1, CA3090618A1);

Collaboration opportunity with Ghent University to further develop the SynAB technology (e.g. for optimized sensitivity or for removal of CER, BEA and ENN from food samples)

References:

Ornelis, V., Raijkovic, A., Sas, B., De Saeger, S., and Madder A. (2018) Development of a Synthetic Receptor for the Food Toxin Beauvericin: A Tale of Carbazole and Steroids. Org Lett. 20, 6368-6371. DOI: 10.1021/acs.orglett.8b02630

Ornelis, V., Raijkovic, A., Sas, B., De Saeger, S., and Madder A. (2019) Counteracting in Vitro Toxicity of the Ionophoric Mycotoxin Beauvericin – Synthetic Receptors to the Rescue. J. Org. Chem. 84, 10422-10435. DOI: 10.1021/acs.joc.9b01665

Contact:

andreas.renz@ugent.be