Edward A. Bayer

Shi-You Ding
Tikva Kulik
Adva Mechaly
Ely Morag
Linda J.W. Shimon

The high-affinity cohesin-dockerin interaction as a model for protein-protein biorecognition

Department of Biological Chemistry

Tel. 972 8 934 2373 **Fax.** 972 8 946 8256
E-mail: ed.bayer@weizmann.ac.il

The cellulosome

Many cellulolytic microorganisms produce intricate multi-enzyme complexes called cellulosomes that efficiently degrade cellulose -- the most abundant organic polymer on Earth. The cellulosomes are composed of a conglomerate of subunits, each of which comprises a set of interacting functional modules. A multi-functional integrating subunit (called scaffoldin) is responsible for organizing the cellulolytic subunits into the multi-enzyme complex. This is accomplished by the interaction of two complementary classes of domain, located on the two separate types of interacting subunits, i.e., a cohesin domain on scaffoldin and a dockerin domain on each enzymatic subunit. The high-affinity cohesin-dockerin interaction defines the cellulosome structure (Fig. 1). The scaffoldin subunit also bears a cellulose-binding domain (CBD) that mediates attachment of the cellulosome to its substrate.

The cohesin-dockerin interaction

We have cloned and expressed individual cellulosomal domains and have analyzed their structure-function relationship via biochemical, molecular, and structural studies. One productive approach has been to determine the crystal structures of the important domains, e.g., the cohesin and CBD. In an alternative, complementary approach, we have analyzed the interaction between recombinant mutant cohesins and mutated dockerin-containing enzymes. The native interaction itself was found to be one of the strongest protein-protein interactions in nature. By comparing the cohesin-dockerin interaction between two different dockerin species, it was concluded that the cross-species interaction is species specific.

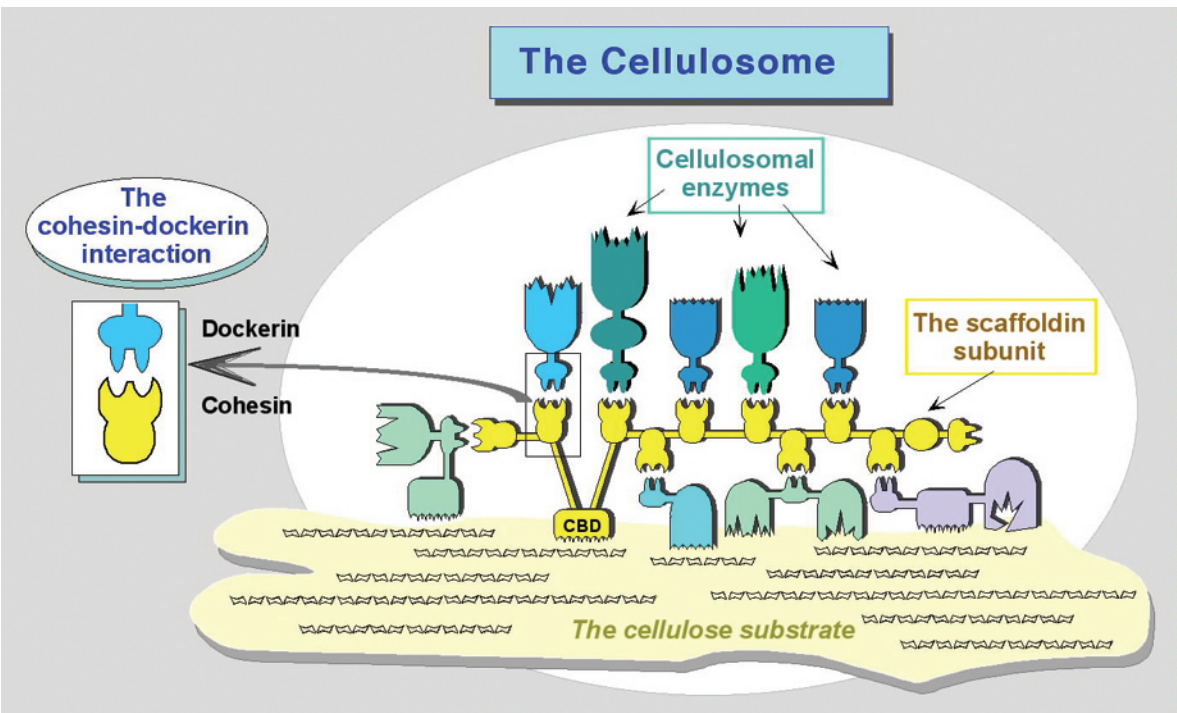

Fig. 1 *Simplified scheme of a typical cellulosome. The scaffoldin subunit (shown in yellow) contains a cellulose-binding domain (CBD) and multiple copies of subunit-binding domains, termed cohesins, interconnected by linker segments. The catalytic subunits (blues, greens) are integrated into the cellulosome complex by the cohesin-dockerin interaction.*

Bioinformatics-based evaluation of the respective dockerin sequences suggested the involvement of a series of recognition residues, which presumably play a critical role in the specificity of the cohesin-dockerin recognition.

Designer cellulosomes -- nanosomes

We originally proposed a new concept for the construction of designer cellulosomes, which comprise recombinant chimaeric scaffoldin constructs and selected dockerin-containing enzyme hybrids, as a conceptual platform for promoting synergistic action among enzyme components. The rationale of such tailored multi-component nanosomes is illustrated in Figure 2. We are currently developing this objective in practical terms by preparing chimaeric scaffoldins that bear multiple copies of cohesins of different specificities. This enables the precise incorporation of complementary dockerin-containing-components into a nanosome complex by simply mixing them in solution together with the chimeric scaffoldin. One of the major unique aspects of this approach is to control on the molecular level the composition and architecture of the nanosome constructs. Once fully developed, the nanosome approach will eventually be appropriate for general use as a molecular "Lego" for application in nanotechnology.

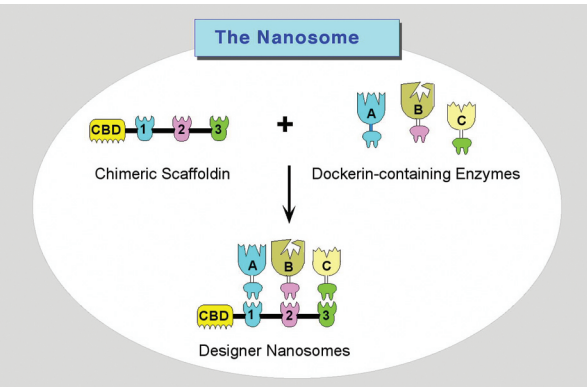

Fig. 2 *Schematic representation of the nanosome concept. A chimaeric scaffoldin contains an optional CBD for targeting to cellulose and multiple cohesin modules (numbered) of different dockerin specificities (color-coded). Incorporation of the complementary dockerin-containing components can then be controlled.*

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Mechaly, A., Fierobe, H.-P., Belaich, A., Belaich, J.-P., Lamed, R., Shoham, Y. and Bayer, E.A. (2001) Cohesin-dockerin interaction in cellulosome assembly: A single hydroxyl group of a dockerin domain distinguishes between non-recognition and high-affinity recognition. J. Biol. Chem., 276, 9883-9888.

Acknowledgements

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Note recent Gordon Research Conference on "Cellulases and Cellulosomes": www.grc.uri.edu/programs/2001/cellul.htm