Elastin-like Recombinamers: Uncovering the Secrets of Elastislet Biomaterials

TOPICS IN DEPTH

Contents

This research project has received funding from the EU's H2020 framework programme for research and innovation under grant agreement n. 646075

Powerful Biomaterials Mimicking Nature

Nature can serve as an extraordinary source of inspiration for scientists and innovators. Several living creatures with unique or attractive features, as well as a great wealth of sophisticated materials displaying remarkable properties can be found in nature.

The examination of natural elastomeric proteins, in particular, inspired scientists to engineer novel synthetic materials with unprecedented functionalities.

An elastomer is any polymeric material that can be stretched without rupture, and then return to its initial conditions. In the plant and animal kingdoms, several proteins display these outstanding elastic properties.

Elastin is one of these.

In the last decades, elastin-inspired materials have been designed and gained increasing importance due to a unique combination of different characteristics: ease handling, design, production and modification, as well as extraordinary biocompatibility.

The Elastin Protein

All body tissues and organs are made of cell and non-cellular components. The extracellular matrix represents the non-cellular component. It provides not only structural support, but also fundamental biochemical and mechanical cues for tissue development and homeostasis. The extracellular matrix is composed of water, polysaccharides and proteins, among which elastin.

Elastin plays an essential role in the functionality of organs and tissues in which elasticity is key, in particular in those that undergo repetitive and reversible deformations, such as the lungs, blood vessels, heart valves and skin, among others. As an elastomeric protein, elastin has the unique property of being able to withstand significant elastic deformations and completely recover its original state when the stimulus is released. Elastin thus provides a wide range of tissues with the necessary strength, elasticity and resilience. It also plays important roles in cellular signalling and regulation.

Bioinspired Materials in Tissue Engineering

Its unique features, along with the fact that it is naturally found in the human body and thus is possibly not recognised as foreign by the immune system, make elastin an attractive material for tissue engineering.

The goal of tissue engineering is to combine materials, cells and/or biologically active molecules into systems that can restore the functionality of diseased, destroyed or damaged tissues and organs.

The holy grail of material design for tissue engineering has long been to create materials that can both help controlling and/or inducing specific cellular behaviours and interact with the host tissue microenvironment without eliciting adverse reactions, such as inflammation, infections, immune rejection and other responses. Indeed, elastin-based materials can match all these requirements.

These materials can be either obtained from nature, from elastin-rich animal tissues, or chemically synthesised. However, the real breakthrough in their design and production was made when genetic and protein engineering took centre stage in their synthesis, opening an ideally infinite range of possibilities for their design, and allowing a tight molecular control over their chemical and physical properties.

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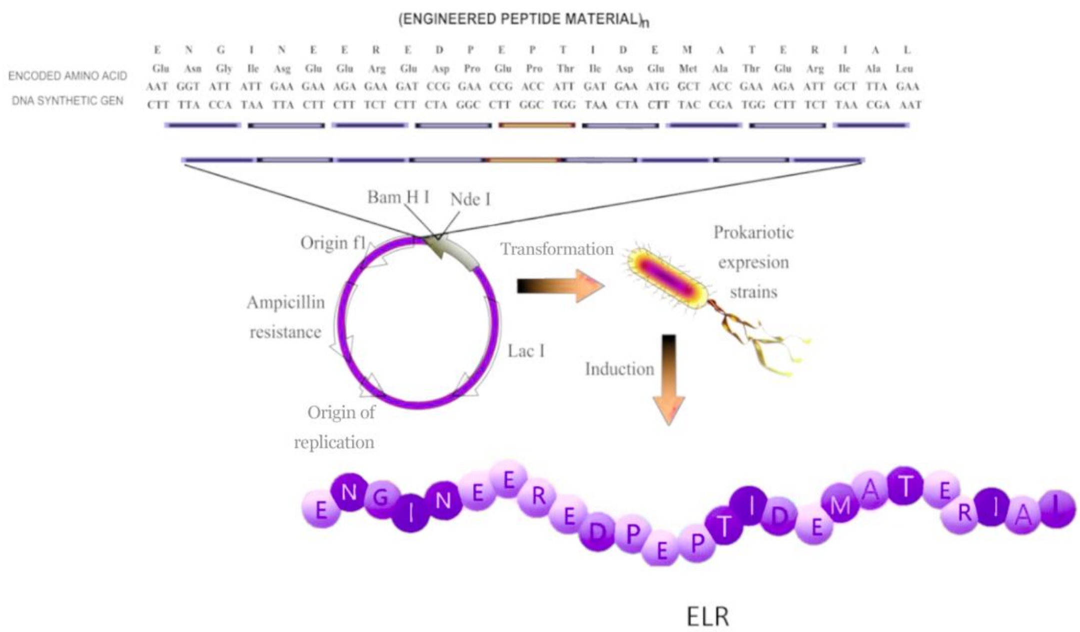
The Genetic Engineering Revolution in Elastin-based Material Design

The development of recombinant DNA technologies in the 1970s provided unprecedentedly powerful tools to study, control and manipulate the genetic blueprint of life.

Living cells use the genetic system to synthesize proteins, by exerting an absolute control over every single protein building block. Genetic engineering provided the tools to exploit this system for biosynthesising desired protein materials in laboratory plates and tubes, with an absolute control over their composition and features.

The study of elastin revealed that the secret of its extraordinary elastic properties lies in the presence of a short sequence of specific building blocks, namely valine-proline-glycine-valine-glycine (VPGVG). This ammino acids' motif is repeated within the protein and is encoded by a specific DNA sequence. Recombinant DNA technologies opened the possibility to use these modules, as well as to combine diverse DNA sequences encoding different protein functional domains, to create complex elastin-inspired synthetic genes. When introduced into a bacterial host like E. coli, and transcribed and translated by the host molecular machines, these recombinant genes lead to the production of recombinant elastin-based protein polymers with tailored properties.

Figure 1



Design of the sequence and production of an elastin like recombinamer by recombinant DNA technologies. Adapted from Rodríguez-Cabello JC et al. Adv Drug Deliv Rev 2018;129:118-133

Hence, an elastin-like recombinamer is a protein material that is produced in bacteria or other microorganisms, from a synthetic recombinant gene of modular design. It contains the peptide sequence responsible for the elastic properties of natural elastin – namely VPGXG, where X can be any amino acid except proline – but its functionalities are expanded according to its envisaged applications, by incorporating specific peptide domains or chemical functionalities into its polymer backbone.

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Within the Elastislet project, elastin-like recombinamers were selected as ideal candidates for the development of an effective islet/islet-like cell encapsulating and immunoisolating system.

To this aim, new molecular architectures were designed and genetically engineered for providing ELR-based biomaterials with specific physical and biological properties. With this protein-based biopolymer as starting material, biocompatible and semipermeable capsules were developed for cell encapsulation. Once implanted, the final system comprising the innovative capsule and the cells will be safe and will allow insulin diffusion from the inside, access to blood supplies and nutrient flows to the transplanted cells.

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