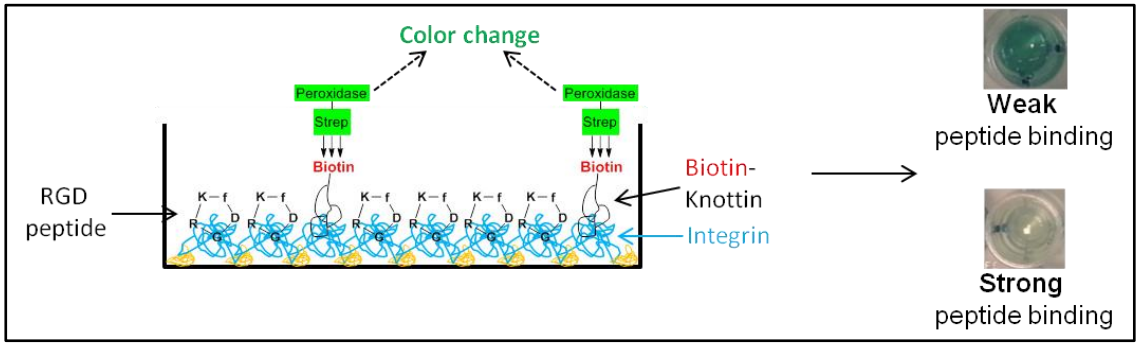
BIOGEL researchers publish a cost-effective method to screen cell-binding peptides

Lelystad (The Netherlands), and Aachen (Germany) 09/05/2017

The extracellular matrix is a network of proteins and sugars that is produced by the cells in the body to further support and direct their function. The cells can attach to this network via proteins present on their membrane, which are called integrins. There are 24 different types of integrins fulfilling different tasks and it depends on the cell type which integrins are expressed and to which extent. The development of integrin-binding peptides has encouraged researchers for more than 20 years to mimic small domains of the extracellular matrix. These peptides can be applied to image and treat different types of cancers, or functionalize synthetic materials to improve cellular adhesion. The shortest cell adhesive peptide domain present in the body is RGD, which is also the most commonly used peptide in research. To increase the binding interaction of RGD, multiple groups have optimized this peptide sequence and different methods have been suggested to analyze its functionality.

Researchers from Pepscan Therapeutics (Lelystad, Netherlands) and DWI (Aachen, Germany) have now collaborated within the Marie Skłodowska-Curie Innovative Training Network BIOGEL to develop a new cost-effective method to screen the binding interaction of RGD peptides to different integrins in high-throughput. Their results are now published in the journal 'Analytical Chemistry'. In their method, a biotin-modified knottin-RGD peptide is used as a high-affinity binding molecule to integrins. When a mixture of the knottin and specific RGD peptide is applied to an integrin-coated surface, the binding interaction of the peptide can be quantified, relative to its ability to block knottin-integrin binding. The amount of bound knottin can be enzymatically quantified via its biotin tag with a lower signal corresponding to a higher affinity of the RGD-peptide. By testing various concentrations of a specific non-labeled RGD peptide, together with a fixed concentration of the biotin-modified knottin, the researchers were able to determine the concentration, at which half of the maximum color intensity is reached. This concentration, called the IC50 value, is characteristic for each peptide and expresses how strong this peptide binds to the respective integrin.

"The main advantage of this method is that for each experiment only a very small amount of an expensive integrin is needed", says Dominik Bernhagen. He is a PhD student working on the BIOGEL project." In addition, the same biotin-modified knottin can be used for three different types of integrin receptors, so that additional expensive compounds like extracellular matrix proteins or antibodies are not required." Peter Timmerman, the CSO of Pepscan continues: "The interesting aspect of the method is that it is suitable to screen large numbers of peptides for integrin-binding, which makes it easier, quicker, and cheaper to find optimized RGD-containing peptides." This novel approach gives an alternative to existing methods and can be applied to discover new integrin-binders, which could then be further used for biomedical research or clinical use. Once strong binders for other peptide motifs, like IKVAV or YIGSR, are identified, the same method could be applied to design peptides to mimic short domains of other extracellular matrix proteins, such as laminin.



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