Heparin-binding domains in elastin-like proteins: a way towards tissue integration?

FACULTY OF SCIENCES
UHASSELT

Niels Geysmans, Sander Driesen, Wanda Guedens, Peter Adriaensens and Geert-Jan Graulus

Biomolecule Design Group, Institute of Materials Research (IMO-IMOMEC), Hasselt University, Belgium

Context

Injectable hydrogels offer an elegant approach to increase stem cell retention following stem cell transplantation. To increase the integration of injectable hydrogels with the surrounding tissue, we envision elastin-like proteins (ELPs) containing heparin-binding domains (HBDs). These positively charged protein domains have been studied as affinity tag and are expected to also interact with negatively charged components in the extracellular matrix (ECM). We studied the interaction of positively charged model systems with hyaluronic acid in an indirect way by measuring changes in the viscosity of hydrogel formulations.

Contact information

+32 11 26 82 67

@BDG_UHasselt

add to contacts

geertjan.graulus@uhasselt.be

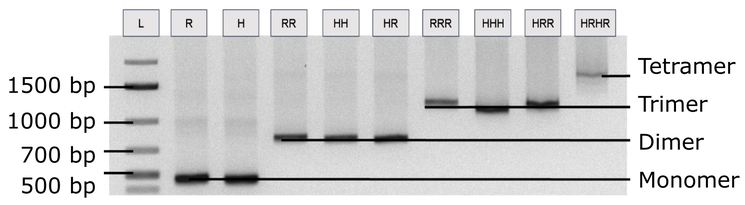
www.uhasselt.be/BDG

HBD ELPs

DNA modification

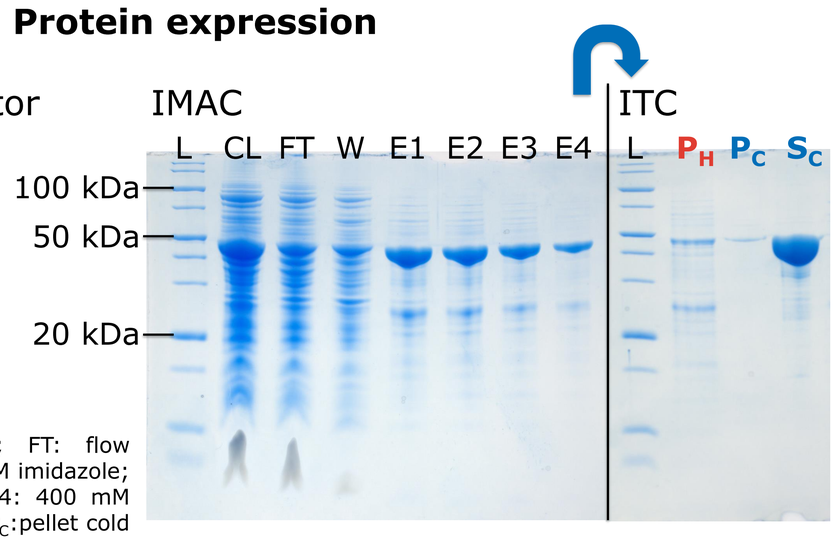
- Basic units via PCR
- Restriction digest
- Assemble (T4 ligas

RGD $(VPGXG)_{15}$ HBD $(VPGXG)_{15}$



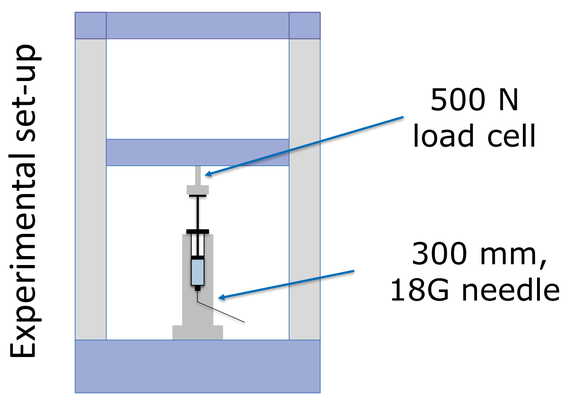
Protein expression

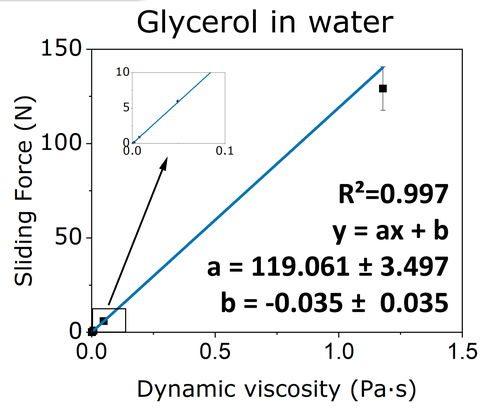
- Expression vector
- Transformation
- Purification
- Analysis

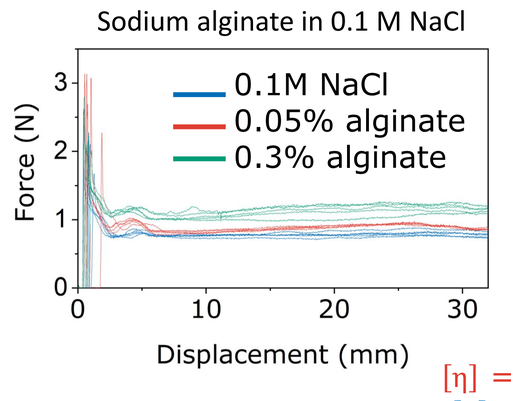


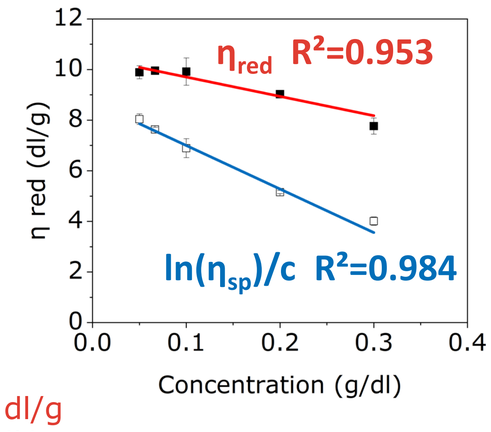
L: ladder; CL: cell lysate; FT: flow through; W: wash; E1: 100 mM imidazole; E2-E3: 250 mM imidazole; E4: 400 mM imidazole, P_H:pellet hot spin; P_C:pellet cold spin; S_C:supernatant cold spin

Mechanical analysers in rheology







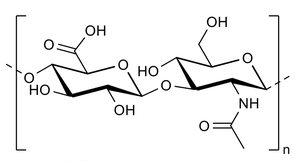


1. External calibration
2. $[\eta] = K(M_W)^{\alpha}$

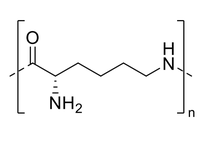
$[\eta]$ = 10.468 dl/g
$[\eta]$ = 8.721 dl/g

M_W (SEC)	130 kDa
M_W (from viscosity)	109-132 kDa

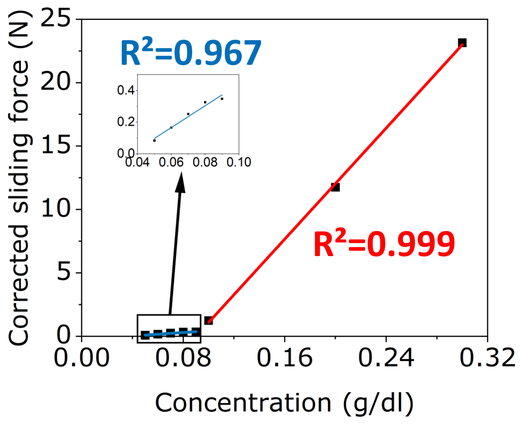
Self-assembly in simplified model systems

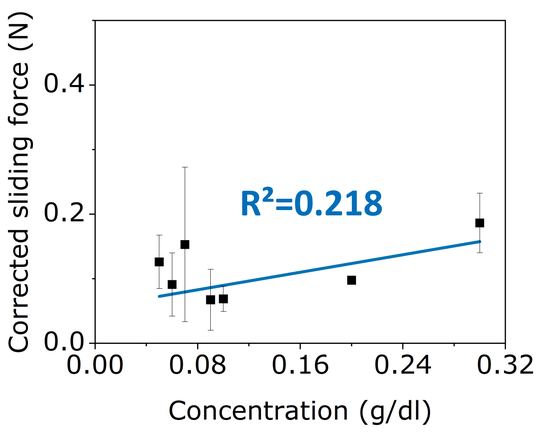


Hyaluronic acid in 0.2M NaCl
MW ≥ 350 kDa

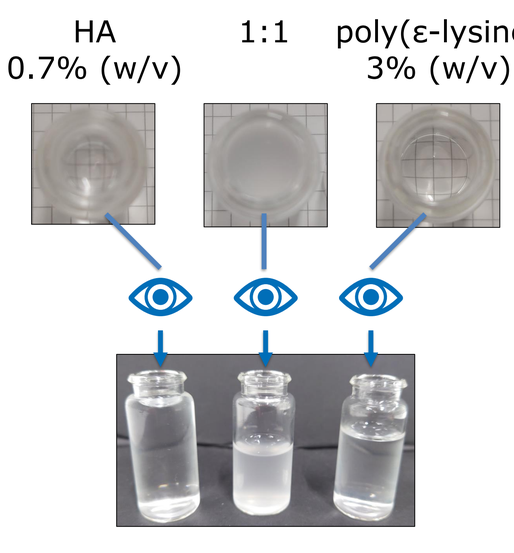


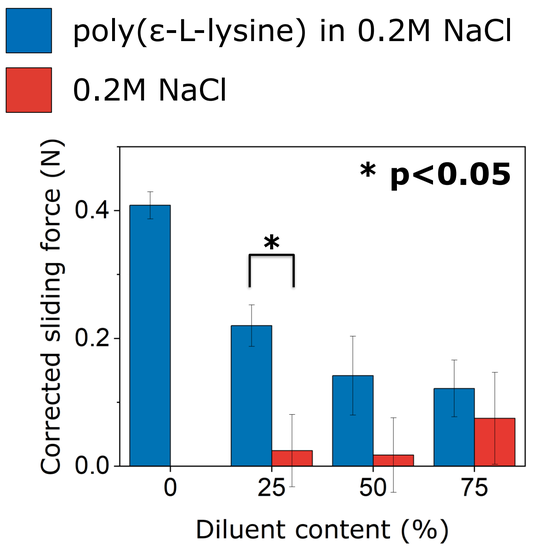
Poly(ε-L-lysine) in 0.2M NaCl
MW 2.5-3.5 kDa





Coarcevation can be observerd visually and increases the corrected sliding force





Conclusions and future perspectives

- Our set-up is sufficiently sensitive to detect self-assembly in dilute aqueous solutions.
- Protein expression needs to be increased to allow for the in-depth analysis of the self-assembly of the HBD domains with negatively charged macromolecules and of the tissue integration of injectable hydrogels based on these components.

Funding information

Our research is supported by the Research Foundation Flanders (FWO, projects 1SB1220N and 1S19023N) and by the special research fund of Hasselt University (BOF-UHasselt, project R-12788).

fwo
UHASSELT