

## Elastin-Like Polypeptides (ELP) Block Co-Polymers

The goal of this study is to develop genetically engineered polypeptides that undergo controlled self-assembly into monodisperse nanoparticulates.

Due to their unique phase behavior, elastin-like polypeptides (ELP) block copolymers can be induced to form micelles by applying a suitable stimulus, such as heat. A library of ELP block copolymers were genetically synthesized, which contain the amino acid sequences (VPGIG)<sub>n</sub> and (VPGSG)<sub>n</sub> of various lengths, n.

Synthetic genes were developed using a recursive directional ligation (RDL) approach where the N-terminal gene of one block copolymer was ligated to a C-terminal ELP gene of another. Plasmid vectors containing the desired constructs were expressed and purified from *E. coli*. The temperature dependent self-assembly of optimized block copolymers was monitored using a DynaPro Plate Reader Dynamic Light Scattering (DLS) instrument to characterize the hydrodynamic radius and polydispersity as a function of temperature.

At the starting temperature of 20°C, individual ELP molecules ( $R_h = 3.2$  nm, MW = 39 kD) predominate in solution (Figure 1a). When the temperature reaches 25°C, a new larger particle with an  $R_h$  of 19 nm was observed (Figure 1b); furthermore, the standard deviation of the micelle radii estimated from the cumulants fit was remarkably narrow (PD = 3.4nm). This larger species persists up to 60°C (Figure 2.) The formation of these particles corresponded to the hydrophobic collapse of the ELP [VPGIG]<sub>n</sub> block. These polypeptide nanoparticles are hypothesized to consist of a hydrophobic core that is stabilized by a hydrophilic shell composed of ELP [VPGSG]<sub>n</sub>.

The automated DLS was a very effective method for observing the in solution formation of polypeptide nanoparticles; furthermore nanoparticle formation corresponded to the transition behavior of the hydrophobic polypeptide block.

This note graciously submitted by S. Janib & J.A. MacKay, Department of Pharmacology and Pharmaceutical Sciences, University of Southern California, Los Angeles, CA.

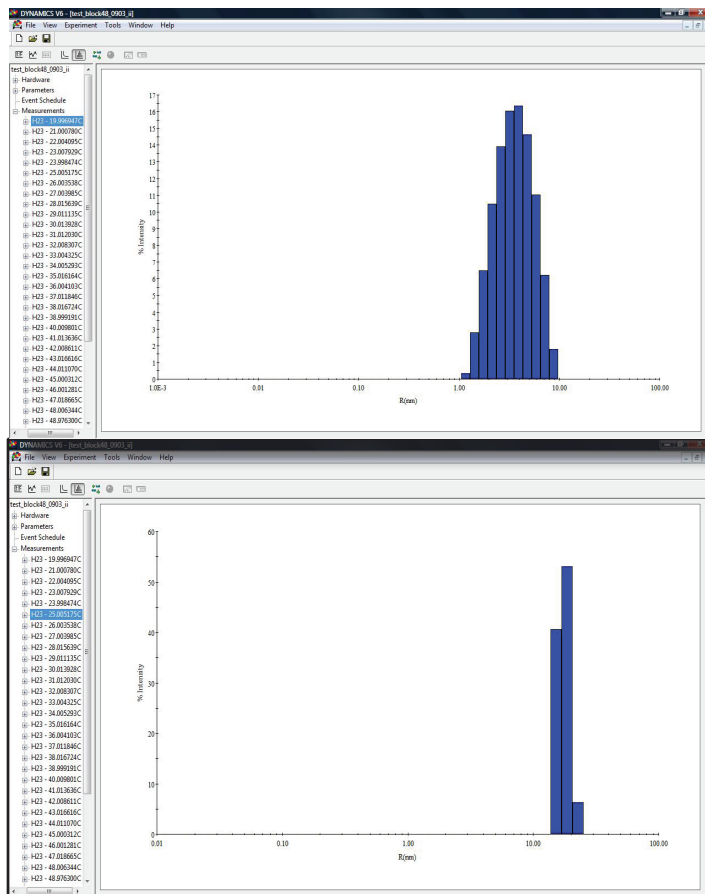


Figure 1. Regularization analysis of ELP block copolymers at (top) 20°C and (bottom) 25°C

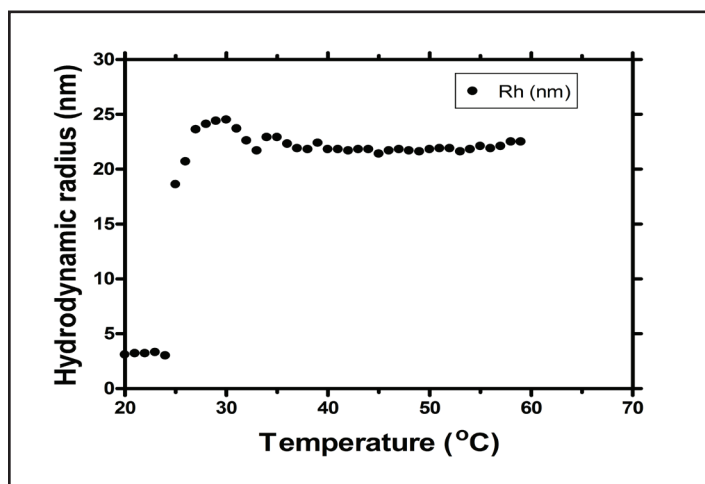
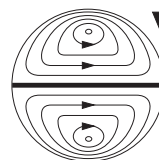


Figure 2. Hydrodynamic radius of ELP block copolymer versus temperature. The DLS data were acquired in PBS at a 25μM ELP concentration.



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