

Synthesis of pH-Responsive Hybrid Copolymers and Their Conjugation with Protein to Combat Myasthenia Gravis

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The main goal of this study is to successfully entrap a protein, to increase its half-life in the body, and to study its activity in *in vivo* experiments.¹

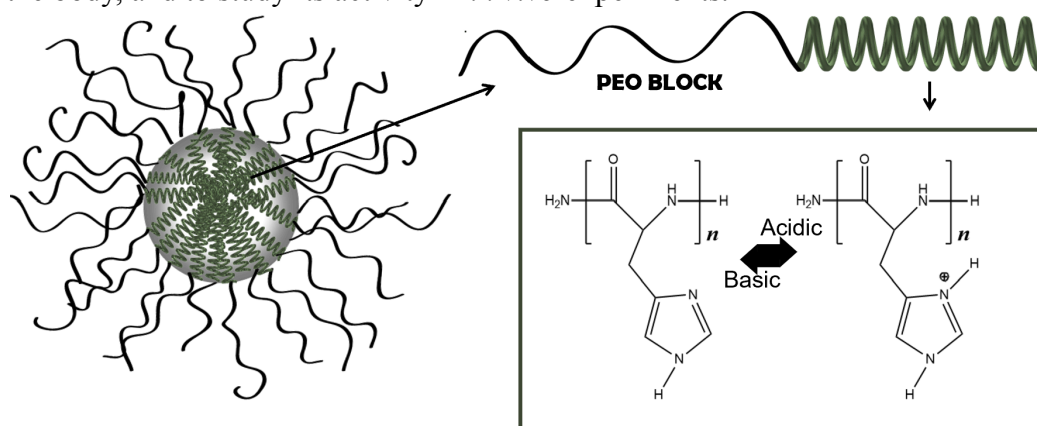


Figure 1: Poly-histidine conformations in acidic and basic environments.

A soluble mutant form of the extracellular domain of the $\alpha 1$ chain of AChR ($\alpha 1$ -ECDm), which represents most of the auto-epitopes involved in Myasthenia Gravis (MG), was used.² To achieve efficient transport of the protein, via the systemic route, a hybrid polypeptide of the type poly(ethylene oxide)-b-poly(L-histidine) (PEG-b-PHIS) was synthesized as shown in Figure 1.³ The property of self-organizing into crown-core micellar structures was exploited.⁴ It was then investigated whether its intravenous administration to rats could safely and effectively treat the autoimmune disease. The *in vivo* experiments confirmed the existence of the protein incorporated into the nanoparticles, as it showed activity. It was studied by electrophoresis by incubating the nanoparticles at various pH, with imidazole to release the protein and with DMSO. However, it was observed that the incubation step of the protein in DMSO affects its shape. The samples were also studied by radioactivity to determine the amount bound.

References:

1. Christina Varfi, Synthesis and Characterization of pH-Responsive Hybrid Copolymers Containing Poly(Ethylene Oxide), Poly(Histidine) and Poly(Glutamic Acid) and Their Complexation with the $\alpha 1$ -ECDm Protein to Combat Myasthenia Gravis, Diplomatic, Dept. Chemistry, EKPA, 2024.
2. Kalamida, D. et al. Muscle and neuronal nicotinic acetylcholine receptors. FEBS J 274, 3799–3845 (2007).
3. Skoulas, D. et al. Polymers (Basel) 9, 208 (2017).
4. Athanasiou, V. et al. ACS Appl Nano Mater 4, 14217–14230 (2021)