Assembly of α-Helical Nanopores for Ultrasensitive Disease Protein Detection

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Synthetic nanopores are promising candidates for single-molecule protein sensing, with α-helical nanopores offering a powerful platform for chemical modifications and tunable selectivity. Here, we report a synthetic α-helical peptide pore, pPorA, which assembles autonomously into octameric pores with both large and small conductance states. Large cyclic sugars bind to small-diameter pores without translocation but traverse through the large-diameter pores, confirming the structural flexibility and size-dependent selectivity of these pores. Furthermore, by utilizing large-diameter pores, we achieved real-time, label-free detection of the conformational states of α-synuclein and its pathological mutants associated with Parkinson's disease. Multiple pathological α-synuclein proteins were simultaneously introduced into the bilayer system and were individually resolved and classified based on their distinct current signatures. The small-diameter pores were utilized to distinguish conformational variants of the mitochondrial peptide Humanin and its disease-associated mutants, providing insight into their roles in the regulation of apoptosis. These findings establish the functional versatility of α-helical peptide pores for complex protein sensing, demonstrating their application in developing next-generation nanopore diagnostics tools.

References:

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