Purification of the MED1 Receptor Interaction Domain

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A class of type II diabetes medication interacts with a nuclear receptor known as PPAR?. While these drugs are effective at managing type II diabetes, however, they have dangerous side effects including heart failure. One way to improve these pharmaceutical drugs is to understand how PPAR? controls the transcription of anti-diabetic genes through interacting with the coregulator MED1. Because MED1 is an intrinsically disordered protein, which makes it difficult to purify and study, research on MED1 has been minimal in current literature and only uses a small domain of the entire protein. We hypothesized that larger portions of MED1 would encompass more binding sites and thus have a higher affinity for PPAR?. To test this hypothesis, we screened various portions of the MED1 protein to determine the impact of size, growth conditions, and purification methods on protein purity when expressed in E. coli cells. These optimized protocols were then implemented in a final trial to compare the effect that the length of MED1 has on the binding affinity of MED1 to PPAR?. This trial provided data that longer regions of MED1 do bind tighter to PPAR?, supporting the hypothesis that domains outside the main interacting region of MED1 contribute to binding. Studying this interaction will lead to a better understanding of how current pharmaceutical drugs behave, and how they can be improved to have fewer side effects.

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