Use AlphaFold2 at SER-CAT for Crystallographic Analyses and Function Research

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Advances in structure prediction by Alphafold2 improve model accuracy significantly to such a level (Jumper et al.: Nature 596:583-589, July 15, 2021; Evans et al.: Protein complex prediction with AlphaFold-Multimer. bioRxiv 2021, https://doi.org/10.1101/2021.10.04.463034) that it could potentially provide a simple way to phase X-ray diffraction data via molecular replacement in cases where a homologous X- ray structure is unavailable. Since the Alphafold2 model is based on the target protein's sequence, the approach addresses model bias associated with the molecular replacement method. The approach would also significantly increase the efficiency of structure production since it is not dependent on isomorphous heavy atom derivatives or anomalous scatterers (e.g., selenomethionine labeling).

More recently, an AI (Artificial Intelligence)-based protein interaction screening and identification method has been developed (Fu et al.: Int. J. Mol. Sci. 2022, 23, 11685), which could significantly speed up the searching process for unknown specific protein-protein bindings by prioritizing a long list of potential binding partners, extending the application of AlphaFold2 far beyond structure predictions. The SER-CAT AlphaFold2 client- server and use of the program for screening potential specific protein-protein bindings will be discussed. Work is supported by the SER-CAT Member Institutions (see www2.ser- cat.org), the University of Georgia Research Foundation, and the Georgia Research Alliance.