Hypusination is a unique modification that occurs exclusively in the protein eIF5A, essential for protein synthesis and cell growth. This process begins with the enzyme deoxyhypusine synthase (DHS), which attaches a part of the spermidine molecule to a specific lysine residue in eIF5A, creating a non-standard amino acid called deoxyhypusine. This is then modified by deoxyhypusine hydroxylase (DOHH) to form hypusine, a crucial component for eIF5A's function.

While hypusination plays a critical role in cell proliferation and is implicated in various diseases, including cancer and neurological disorders, existing inhibitors lack the specificity needed for precise targeting of this pathway. The current project seeks to address these limitations by developing **innovative covalent inhibitors** that can specifically target DHS. These inhibitors are designed to form strong, covalent bonds with DHS, offering a novel approach that promises greater specificity and effectiveness than previous methods.

In addition to these new inhibitors, the project will utilize advanced fragment screening techniques, including the **creation of a specialized library tailored to target DHS more precisely**. This approach represents a significant leap forward from traditional screening methods, enabling the discovery of highly specific compounds that interact with DHS in novel ways.

Furthermore, this research will employ **cutting-edge tools to map the interactome of DHS** using the BioID method. This technique will allow us to identify and understand the network of proteins that interact with DHS within the cell, offering new insights into its regulation and function.

Overall, this project introduces several innovative strategies to advance our understanding of the hypusination pathway. By developing new covalent inhibitors, employing advanced screening techniques, and exploring the DHS interactome, this research aims to create powerful new tools that will enable deeper exploration of hypusination and its role in health and disease.