Computational Investigation of Peptide Binding to Fibrin for Molecular Imaging of Post-Surgical Abdominal Adhesions

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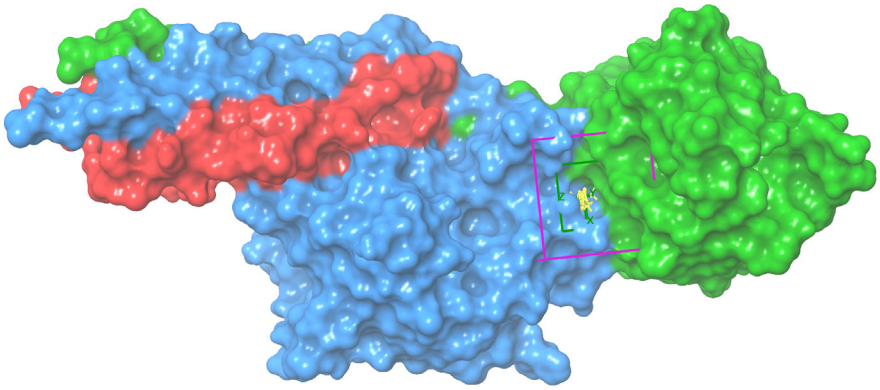
Abdominal adhesions are bands of fibrous scar tissue that can connect tissues and organs that normally slide across each other. Complications can cause chronic pain, infertility, and many additional therapeutic costs. Current clinical imaging techniques, such as MRI and ultrasound, are ineffective for early detection, so exploratory surgeries are the only method to identify their exact location. Imaging is thus crucial for identifying adhesion location and formation, and for conducting treatment studies. Fibrin is a major component in early adhesion formation and consequently is an attractive molecular target. The goal of this project is to design optimized peptides that bind to fibrin for tissue targeting. Analysis of fibrin binding sites was performed using data from literature and the Protein Data Bank (PDB). A reference fibrin-ligand structure and complex of interest were aligned and visualized in Maestro, a 3D visualization software, to compare peptide binding locations. The fibrin structure was also analyzed in FTMap, a server that locates binding hot spots on the surface of proteins. Unbiased conformers of the peptides were generated and docked in the previously identified hot spots to ensure accurate protocol. The docked conformers also function as a control to compare binding affinities of engineered peptides. The project provides data on peptide-fibrin binding predictions and serves as a foundation to engineer an optimized peptide for tissue targeting. The engineered peptide will provide a basis for further research into a targeted contrast agent to visually detect newly forming adhesions.



Monomer of fibrin structure 1FZG with docking box centered on the largest hot spot cluster (yellow). Structure is colored by chain with the gamma chain in green, beta chain in blue, and alpha chain in red.