Design of drugs to treat influenza A virus infections and tissue fibrosis.

M2 is the target of the anti-influenza drugs amantadine and rimantadine. Although this class of compounds was used to treat influenza A virus infections for several decades, currently circulating strains of the virus are largely resistant to these drugs. Structural and molecular dynamics investigations of the channel have shown the mechanism by which protons are stabilized as they transit through the pore, leading to a new understanding of drug-inhibition as well as the development of new classes of drugs that address the problem of drug-resistance.

The second topic addresses the need for effective therapies specifically targeting fibrosis, which is a major cause of organ failure. Transforming growth factor β is a central mediator of fibrotic processes, and its activation thorough αv integrins has been increasingly important in therapeutic development. We have developed a potent and highly specific small molecule inhibitor of the αvβ1 integrin and show that this inhibitor completely inhibits TGFβ activation by primary fibroblasts from several organs. We also show that the inhibitor is therapeutically effective *in vivo* in mouse models of lung, liver and kidney fibrosis. This study suggests that αvβ1 inhibitors may be useful therapeutics for treating fibrotic diseases of multiple organs.