

Structural Studies of Membrane Proteins and Drug Targets

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Introduction: High resolution structural information is critical to an understanding of drug mechanisms. We have focused on two areas of pharmacological interest: Mechanism of inhibition of prostaglandin H2 synthase (PGHS) by non-steroidal anti-inflammatory drugs (NSAIDs), and the mechanism of action of glycopeptide antibiotics.

Results and Conclusions: Structures have been obtained for complexes of PGHS with four different NSAIDs, including the ubiquitously used ibuprofen. This structural information has allowed us to critically evaluate long-standing hypotheses that seek to explain differences in drug action. Additionally, we have determined a high-resolution structure for the aglycon of the antibiotic vancomycin. Comparison of this structure with that of the intact molecule has revealed the conformational consequences of sugar addition.

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