P-glycoprotein: new insights into structure, physiological function, regulation and alterations in disease

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Abstract The multidrug resistance phenomenon presents a major threat to the pharmaceutical industry. This resistance is a common occurrence in several diseases and is mediated by multidrug transporters that actively pump substances out of the cell and away from their target regions. The most well-known multidrug transporter is the P-glycoprotein transporter. The binding sites within P-glycoprotein can accommodate a variety of compounds with diverse structures. Hence, numerous drugs are P-glycoprotein substrates, with new ones being identified every day. For many years, the mechanisms of action of P-glycoprotein have been shrouded in mystery, and scientists have only recently been able to elucidate certain structural and functional aspects of this protein. Although Pglycoprotein is highly implicated in multidrug resistant diseases, this transporter also performs various physiological roles in the human body and is expressed in several tissues, including the brain, kidneys, liver, gastrointestinal tract, testis, and placenta. The expression levels of P-glycoprotein are regulated by different enzymes, inflammatory mediators and transcription factors; alterations in which can result in the generation of a disease phenotype. This review details the discovery, the recently proposed structure and the regulatory functions of Pglycoprotein, as well as the crucial role it plays in health and disease.

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