Pharmacogenomics of GPCR Drug Targets - DTU Orbit (09/12/2018)

Pharmacogenomics of GPCR Drug Targets

Natural genetic variation in the human genome is a cause of individual differences in responses to medications and is an underappreciated burden on public health. Although 108 G-protein-coupled receptors (GPCRs) are the targets of 475 (∼34%) Food and Drug Administration (FDA)-approved drugs and account for a global sales volume of over 180 billion US dollars annually, the prevalence of genetic variation among GPCRs targeted by drugs is unknown. By analyzing data from 68,496 individuals, we find that GPCRs targeted by drugs show genetic variation within functional regions such as drug- and effector-binding sites in the human population. We experimentally show that certain variants of μ-opioid and Cholecystokinin-A receptors could lead to altered or adverse drug response. By analyzing UK National Health Service drug prescription and sales data, we suggest that characterizing GPCR variants could increase prescription precision, improving patients’ quality of life, and relieve the economic and societal burden due to variable drug responsiveness.

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