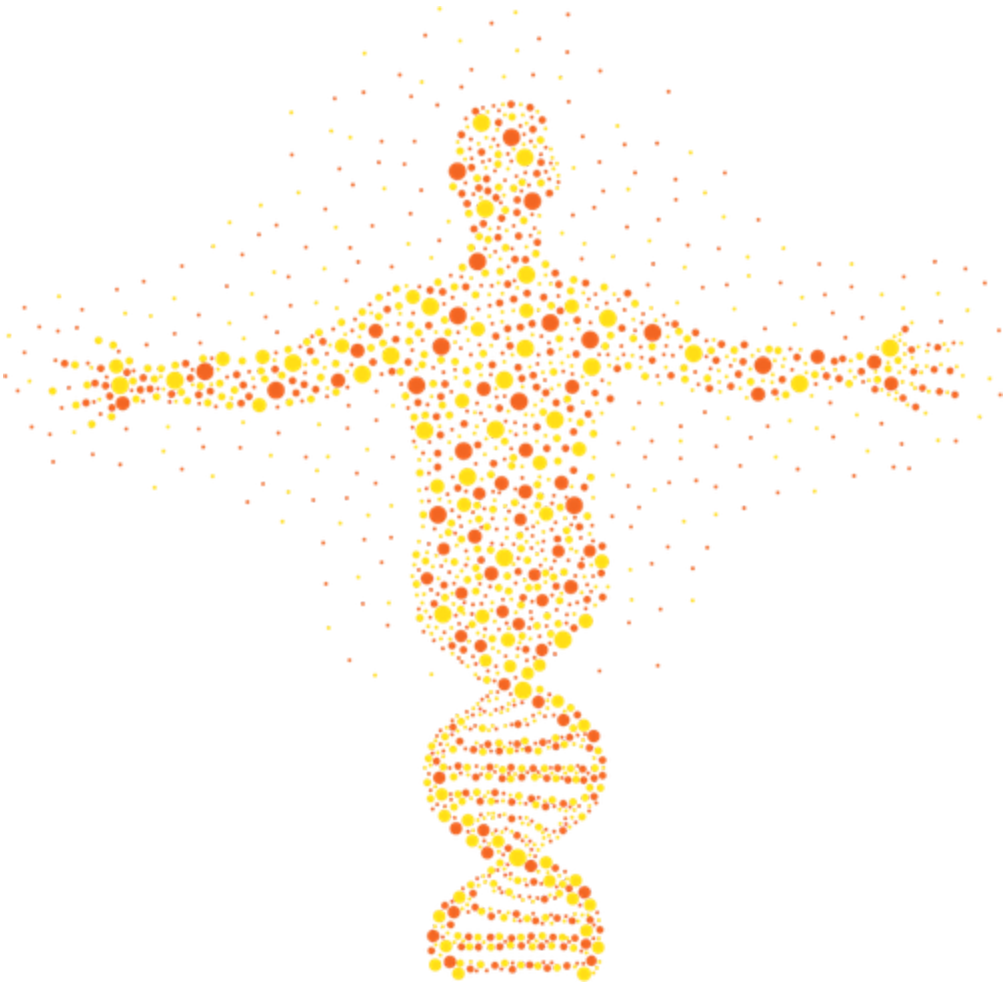

Pharmacogenetic testing for Suxamethonium (Succinylcholine)

Pharmacogenetic testing for Suxamethonium (Succinylcholine)

Suxamethonium (Succinylcholine) is an adjunct to general anesthesia, to facilitate tracheal intubation, and to provide skeletal muscle relaxation during surgery or mechanical ventilation. Succinylcholine, is a fast-acting depolarising muscle relaxant and is widely used in clinical settings. Succinylcholine is an analog of the neurotransmitter acetylcholine. The molecule binds non-competitively and therefore the binding cannot be reversed and recovery is spontaneous.

The molecule is metabolised by the BChE enzyme encoded by the *BCHE* gene. Patients with normal *BCHE* gene hydrolyze 90% of the injected drug dose before it reaches nerve synapse in the muscle. In contrast, subjects with an abnormal BChE gene results in a huge overdose leading to prolonged muscle paralysis, a serious and potentially lethal adverse drug response. Apart from succinylcholine containing drugs Quelicin & Anectine, the gene also is involved in metabolism of mivacurium, ester local anesthetics particularly chloroprocaine.

The prevalence of *BCHE* deficiency varies with population as well as ethnic subgroups. The incidence is approximately 1 in 100,000 individuals of European or American descent being homozygous for the variant, whereas some ethnic subgroups, including the *Vysya* community of India have a high prevalence of approximately 4%[1].

Apart from genetic factors, acquired conditions affecting BChE enzyme activity include liver diseases like cirrhosis, acute hepatitis, liver abscesses; renal diseases; malnutrition; pregnancy; HELLP syndrome; Malignancy like hepatic carcinoma, lung, gastrointestinal, genitourinary malignancies and breast cancer; cardiopulmonary bypass.

The reduction seen in many of the acquired conditions may be of little clinical significance but in combination with a genetic variant, relevant condition, or presence of a particular drug, the reduction may be a contributing factor to adverse side effect.

Pharmacogenetic testing is recommended on the US FDA Drug label

The US FDA-approved label warns that individuals who are carriers of the atypical variant of the plasma cholinesterase gene (*BCHE*) are at risk of prolonged apnea if administered succinylcholine. The US FDA-approved label[2] contraindicates succinylcholine for individuals carrying one of many genetic variants known to increase the risk of adverse side effect.

[1] Soliday FK, Conley YP, Henker R. Pseudocholinesterase deficiency: a comprehensive review of genetic, acquired, and drug influences. AANA J. 2010 Aug;78(4):313-20. Review. PubMed PMID: 20879632.

[2] The US FDA approved drug label as well as recommendations are available on the PharmGKB website https://www.pharmgkb.org/chemical/PA451522

Genetic variants associated with BChE deficiency

A number of genetic variants are associated with BChE deficiency. ClinVar, a comprehensive resource for genetic variants associated with human traits lists over 31 pathogenic variants.

The prevalent genetic variants include rs104893684 (NC_000003.11:g.165547818A>G) rs28933390 (NC_000003.11:g.165547569C>A), rs12198557 (NC_000002.11:g.184161120C>G), rs28933389 (NC_000003.11:g.165548010G>A), rs121918558 (NC_000003.11:g.165548355T>A), rs201820739 (NC_000003.11:g.165548394C>T), rs1799807 (NC_000003.11:g.165548529T>C) and rs121918556 (NC_000003.11:g.165504043T>A) in *BCHE* gene.

dbSNP rsID of variants	Amino Acid Translation (NP_000046.1)	Phenotype	Alternate Names
rs28933389	Thr271Met	Resistant to inhibition by sodium fluoride; decreases BChE enzyme activity	F- Variant
rs28933390	Gly418Val	Resistant to inhibition by sodium fluoride; decreases BChE enzyme activity	F-Variant
rs1799807	Asp98Gly	Resistant to inhibition by dibucaine; decreases the affinity of BChE enzyme for SCH	A-Variant
rs121918558	Tyr156Cys	Significant decrease in BCHE levels	
rs104893684	Leu335Pro	BChE is absent from plasma; found only in the Vysya of India	S-Variant
rs121918557	Leu358Ile	Resistant to inhibition by sodium fluoride and dibucaine; decreases BChE enzyme activity; found only in Japan	F-Variant
rs201820739	Gly143Asp	Deficiency of butyrylcholine esterase	
rs121918556	Glu525Val	Causes a 66% reduction in circulating enzyme and decrease in BChE activity	J-variant

Table 1. Summary of the prevalent genetic variants in BChE gene. A type variants are the atypical or the dibucaine resistant, F type variants are fluoride resistant while ,S variants are silent variants.

Referring your patient for Pharmacogenetic testing of BChE gene

Pharmacogenetic testing in research mode for succinylcholine is available through the GOMED programme for the prevalent variant rs104893684 in South Asian Populations.

Additional variants listed above may be tested on request of the investigator.

Request a test for your patient

The tests can be **requested only by Registered and practicing Clinicians**. If you are a patient, you could contact your consulting clinician to refer you for genetic screening.

For further details, request forms and procedures, visit us at http://gomed.igib.in/scoline