**S1 Table. Principles and training datasets of six evaluated prediction tools.**

| Tool name | Version | Principle | Training dataset | Reference |
|---|---|---|---|---|
| CADD | 1.2 | Logistic regression | High-frequency human-derived variants 14.7 million observed / 14.7 million simulated | [24] |
| DANN | 2014-11-14 | Deep neural network | High-frequency human-derived variants 14.7 million observed / 14.7 million simulated | [26] |
| FATHMM | 2015-02-25 | Support vector machine | HGMD (heritable germline), 1000 Genome (MAF ≥ 1%) 12,438 deleterious / 24,064 neutral | [27] |
| FitCons | 1.01 Cell type: H1 hESC | Evolutionary fingerprints | No training dataset | [28] |
| FunSeq2 | 2.1.2 | Weighted scoring system | No training dataset | [32] |
| GWAVA | 1.0 Model: region | Random forest | HGMD (regulatory), 1000 Genome (MAF ≥ 1%) 1,614 deleterious / 5,027 neutral | [25] |

CADD – Combined Annotation Dependent Depletion, DANN – Deleterious Annotation of Genetic Variants using Neural Networks, FATHMM – Functional Analysis through Hidden Markov Models, FitCons – Fitness Consequences of Functional Annotation, GWAVA – Genome-Wide Annotation of Variants, hESC – human embryonic stem cells, HGMD – The Human Gene Mutation Database, MAF – Minor allele frequency