

**Table S1:** The prediction outcomes for the nsSNPs effect on ADAM33 protein by MutPred server.

| SNP ID       | AAS   | Probability of deleterious amino acid substitution | Top 5 features   |
|--------------|-------|--|--|
| rs773091023  | P678L | 0.800  | Altered Transmembrane protein<br>Loss of Loop<br>Gain of Disulfide linkage at C680   |
| rs764301730  | C671R | 0.951  | Altered Metal binding<br>Altered Transmembrane protein<br>Gain of Catalytic site at C671<br>Loss of Disulfide linkage at C671  |
| rs751597707  | C669G | 0.937  | Altered Metal binding<br>Altered Transmembrane protein<br>Altered Stability<br>Gain of Disulfide linkage at C671<br>Gain of Catalytic site at C669   |
| rs368984072  | G661R | 0.897  | Altered Metal binding<br>Altered Transmembrane protein<br>Loss of Disulfide linkage at C663  |
| rs777553708  | C637Y | 0.943  | Altered Transmembrane protein<br>Loss of Disulfide linkage at C637<br>Altered Metal binding<br>Gain of Strand<br>Altered Disordered interface  |
| rs1334863089 | C631F | 0.953  | Altered Metal binding<br>Altered Transmembrane protein<br>Loss of Disulfide linkage at C631<br>Gain of Catalytic site at C631  |
| rs754867141  | C606S | 0.857  | Loss of Disulfide linkage at C606<br>Altered Metal binding<br>Altered Transmembrane protein<br>Altered Stability<br>Gain of O-linked glycosylation at T605<br>Gain of Catalytic site at C606 |
| rs754867141  | C606Y | 0.915  | Loss of Disulfide linkage at C606<br>Altered Metal binding<br>Altered Transmembrane protein<br>Gain of Catalytic site at C606  |
| rs915448220  | C573Y | 0.953  | Altered Metal binding<br>Altered Transmembrane protein<br>Gain of Strand<br>Gain of Catalytic site at C573<br>Loss of Disulfide linkage at C573  |
| rs1432549895 | C519R | 0.940  | Loss of Disulfide linkage at C519<br>Gain of Catalytic site at C519<br>Altered Transmembrane protein<br>Altered Metal binding<br>Loss of Pyrrolidone carboxylic acid at Q524                 |
| rs1262246273 | Y513C | 0.898  | Altered Transmembrane protein<br>Gain of Intrinsic disorder<br>Loss of Disulfide linkage at C514<br>Loss of Strand<br>Altered Ordered interface  |
| rs1203116461 | P496L | 0.668  | Altered Transmembrane protein  |

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|              |       |       | Gain of Helix<br>Loss of Strand<br>Loss of Loop<br>Altered Metal binding   |
| rs757567846  | D483A | 0.839 | Altered Metal binding<br>Gain of Disulfide linkage at C482<br>Altered Transmembrane protein  |
| rs1424975479 | C482F | 0.900 | Altered Metal binding<br>Loss of Disulfide linkage at C482<br>Altered Transmembrane protein<br>Loss of Pyrrolidone carboxylic acid at Q477                                   |
| rs1165412077 | C482S | 0.794 | Altered Metal binding<br>Loss of Disulfide linkage at C482<br>Altered Transmembrane protein<br>Loss of Pyrrolidone carboxylic acid at Q477<br>Gain of Catalytic site at C482 |
| rs779669835  | R476C | 0.834 | Altered Metal binding<br>Loss of Disulfide linkage at C475<br>Loss of Pyrrolidone carboxylic acid at Q477<br>Altered Transmembrane protein                                   |
| rs748720838  | C475G | 0.942 | Altered Metal binding<br>Loss of Disulfide linkage at C475<br>Loss of Pyrrolidone carboxylic acid at Q477<br>Altered Transmembrane protein                                   |
| rs528261077  | G472V | 0.828 | Altered Metal binding<br>Gain of Disulfide linkage at C475<br>Gain of Pyrrolidone carboxylic acid at Q477  |
| rs1378161696 | C463Y | 0.915 | Altered Metal binding<br>Loss of Intrinsic disorder<br>Altered Transmembrane protein<br>Gain of Disulfide linkage at C462  |
| rs768654352  | G460R | 0.856 | Gain of Helix<br>Altered Metal binding<br>Gain of Disulfide linkage at C457<br>Altered Transmembrane protein<br>Gain of Pyrrolidone carboxylic acid at Q456                  |
| rs1192357091 | C444S | 0.852 | Altered Metal binding<br>Loss of Disulfide linkage at C444<br>Altered Transmembrane protein<br>Gain of N-linked glycosylation at N448  |
| rs1192357091 | C444Y | 0.914 | Altered Metal binding<br>Loss of Intrinsic disorder<br>Loss of Disulfide linkage at C444<br>Altered Transmembrane protein<br>Gain of N-linked glycosylation at N448          |
| rs777252478  | C439Y | 0.790 | Loss of Intrinsic disorder<br>Altered Metal binding<br>Loss of Disulfide linkage at C444   |
| rs1321728445 | C431S | 0.881 | Altered Metal binding<br>Gain of Strand<br>Gain of B-factor<br>Altered Transmembrane protein<br>Loss of Disulfide linkage at C431  |
| rs747255442  | G428C | 0.813 | Altered Metal binding<br>Altered Transmembrane protein   |

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|--------------|-------|--------|--|
|              |       |        | Gain of Disulfide linkage at C433  |
| rs776082098  | C420Y | 0.917  | Loss of Intrinsic disorder<br>Altered Metal binding<br>Gain of Strand<br>Altered Transmembrane protein<br>Loss of Disulfide linkage at C420              |
| rs751613984  | C388Y | 0.884  | Altered Metal binding<br>Altered Disordered interface<br>Altered Transmembrane protein<br>Loss of Disulfide linkage at C388<br>Gain of Sulfation at C388 |
| rs1313175203 | C371Y | 0.963  | Altered Metal binding<br>Gain of Strand<br>Loss of Disulfide linkage at C371<br>Altered Transmembrane protein<br>Gain of Catalytic site at C371          |
| rs764090883  | C371R | 0.971  | Altered Metal binding<br>Gain of Intrinsic disorder<br>Gain of Strand<br>Loss of Disulfide linkage at C371<br>Altered Transmembrane protein              |
| rs1297854732 | C360R | 0.882  | Altered Metal binding<br>Gain of Strand<br>Loss of Disulfide linkage at C360<br>Gain of Allosteric site at H355<br>Loss of Catalytic site at H355        |
| rs1351880201 | D219V | 0.9355 | Altered Ordered interface<br>Altered Metal binding<br>Altered Transmembrane protein<br>Altered Disordered interface<br>Loss of Sulfation at Y215         |