**Supplementary 3.** Predicted stability changes (∆∆G in kcal/mol) in IRS1 protein structure upon the selected mutations.

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| --- | --- | --- |
| **Prediction of Protein stability webservers**  | **Effect on protein stability for mutation P948L** | **Effect on protein stability for mutation R1221C** |
| PrempS server | Decreased (ΔΔG=0.3) | Decreased (ΔΔG=0.59) |
| MAESTRO | Decreased (ΔΔG=0.15) | Decreased (ΔΔG=0.338) |