Accessible Surface Area and the Prediction of the Phenotypes of Missense Mutations

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Abstract

Distinguishing between harmful and benign genetic variations is fundamental to our understanding of the relationship between genome and disease in general and for personalized medicine in particular. We investigated the relationship between predicted change in RASA and the phenotype of a missense mutation (MM). The ASAquick program was used to obtain RASA predictions for the original and mutated sequence and a parameter, δ , was introduced to assess the change in RASA for a given MM. We find that predicted RASA shows a robust, intricate signal with respect to genetic variation and that changes in RASA between variants can form a basis for a simple and quick predictor of the effect of MMs. Furthermore, we find that for hydrophobic residues, increase in the RASA corresponds to an increase in the likelihood that a MM would be harmful. For hydrophilic residues we find that a decrease in the RASA corresponds to a likelihood that a MM would be harmful. We also find that the size of the change in predicted RASA plays a role in determining the effect of a given MM. In future work we plan to use these results in developing more sophisticated forms of MM phenotype predictors.

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