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Method to predict immunogenic double-stranded RNA burden

Stanford researchers developed a system that uses an individual's genetic information to predict autoimmune/inflammatory disease risk. Predictions made can be used to identify suitable candidates for precision therapies targeted at the double-stranded RNA (dsRNA) sensing pathways. Immunogenic dsRNAs are linked to inflammation in about 14% of autoimmune and inflammatory disease patients. Predicting disease risk using dsRNA burden identifies individuals suited for precision therapies targeting dsRNA-sensing pathways.

Stanford researchers have shown that increased dsRNA levels are strongly correlated with a higher risk for autoimmune and inflammatory diseases. Hence, they developed a system that uses genetic information to predict immunogenic dsRNA levels. The system collects genetic information and uses it to calculate an immunogenic dsRNA score (IDS). The system then compares the IDS score to IDS thresholds based on known IDS values for a given disease to generate predictions for disease risk. For a given individual and tissue/cell type, a predicted IDS higher than the corresponding IDS threshold indicates high risk.

Stage of Development: Prototype
Stanford researchers continue to optimize the model and use it to develop small molecule inhibitors.

Applications

- **Autoimmune/Inflammatory Disease Screening** including inflammatory bowel disease, rheumatoid arthritis, psoriasis, lupus, coronary artery disease, etc.
- **Precision Medicine and Treatment Development** - autoimmune disease patient stratification for targeted immunogenic dsRNA sensing pathways

therapeutics.

Advantages

- More **precise and specific** than conventional methods:
  - IDS prediction at the tissue/cell type level as opposed to conventional polygenic risk score (PRS) methods.
  - Identifies specific potential disease mechanisms for a given individual with high dsRNA burden, which is critical for precision treatment.
  - The method is based on a very well-studied and specific immunogenic dsRNA sensing pathway.

Publications

- Li, Q., Gloudemans, M. J., Geisinger, J. M., Fan, B., Aguet, F., Sun, T., Ramaswami, G., Li, Y.I., Ma, J.B., Pritchard, J.K. and Montgomery, S.B., & Li, J. B. (2022). RNA editing underlies genetic risk of common inflammatory diseases. *Nature, 608*(7923), 569-577. doi: 10.1038/s41586-022-05052-x

Patents

- Published Application: WO2023239781

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