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Quantitative AML patient risk assessment using RNA signatures associated with sensitivity and resistance to immune cell killing

Stanford researchers have discovered RNA signatures that can be used to predict patient outcomes and identify optimal treatments in acute myeloid leukemia.

Acute myeloid leukemia (AML) is the most common leukemia in adults, with over 20,000 new cases a year in the US and a five-year overall survival rate of only 27%. While reliable methods for predicting patient outcomes in AML could aid clinical decision making by *e.g.* predicting which patients would benefit from more aggressive treatment, AML risk is currently evaluated by a complex combination of factors including age, patient performance status, cytogenetics, and medical history. This method is unreliable particularly for the 30% of patients that lack genetic abnormalities associated with clinical outcomes.

To address this, Stanford researchers discovered transcriptional programs in AML that are associated with either improved or worse patient outcomes. Researchers treated AML patient cells with human immune cells, identifying subsets of AML cells that are either sensitive or resistant to immune cell killing. Immune-resistant AML cells were found to express RNA transcripts associated with poor survival rates in a large database of AML patient transcriptomes. Better and poorer patient outcomes could be predicted from the expression of RNAs associated with sensitivity and resistance to immune cell killing.

Stage of Development
Proof of concept: AML patient cells that are resistant to immune cell killing in vitro express transcripts associated with poorer patient outcomes, while patient cells that are sensitive to immune cell killing express transcripts associated with improved

outcomes.

Applications

- Molecular diagnostic tests for AML patient risk stratification
- Pre-clinical research in AML

Advantages

- More quantitative and reliable than current methods for patient risk assessment in AML
- Easy to implement using established workflows for RNA sequencing or qPCR
- Can be performed non-invasively from a peripheral blood sample or from diagnostic bone marrow aspirate (already used to diagnose AML)

Publications

- Ece Canan Sayitoglu, Bogdan A. Luca, et al. (2023). AML/T cell interactomics uncover correlates of patient outcomes and the key role of ICAM1 in T cell killing of AML. BioRvix, 2023.09.21.558911.

Innovators

- Maria-Grazia Roncarolo
- Alma-Martina Cepika
- Ece Sayitoglu
- Bogdan Luca

Licensing Contact

Eileen Lee

Email