Novel predictive biomarker to determine AML patient sensitivity to MDM2 inhibitors.

THE PROBLEM

Acute myeloid leukaemia (AML) is a lethal malignancy with an overall 5-year survival rate of just 25%. Cytarabine-based chemotherapy has been the standard-of-care for AML for decades despite poor outcomes, and as such new therapeutics are urgently required. Pharmacological inhibition of MDM2/4 has shown promise in this role, with a number of organisations currently in phase I-III clinical trials with their lead candidates. Initial data has shown that combining this approach with cytarabine can lead to durable responses, however only in an as yet undefined subset of patients. Identification of the patients most likely to successfully respond to MDM2/4 inhibition, particularly when in combination with cytarabine, is the current challenge for the market.

THE TECHNOLOGY

Our researchers have identified a novel biomarker of MDM2/4 inhibitor and cytarabine efficacy in AML.

In new data published in *Leukaemia*, biomarker expression strongly correlated to MDM2 inhibitor (Nutlin-3a) sensitivity across NCI-60 cancer cell lines comprising 9 distinct cancer types (Fig.1), as well as in cytarabine-treated AML patients (Fig.2). AML patients exhibit clear bimodal expression delineating them into 'biomarker-high' and 'biomarker-low' subgroups (Fig.3). The biomarker demonstrated a higher positive predicted value (PPV) than current gold standard MDM2/4 inhibitor biomarker (and direct target) p53.

SCIENTIFIC PUBLICATIONS

Vu T, Wang K, Stoelzel F, Ehninger G, Molloy TJ, Ma DDF. *miR-10a as a therapeutic target and predictive biomarker for MDM2 inhibition in acute myeloid leukemia*. Leukemia. (link)

IP POSITION

This technology is the subject of an Australian provisional patent application, and was developed by Prof David Ma, and Dr Timothy Molloy of the St Vincent's Centre for Applied Medical Research

Figure 1

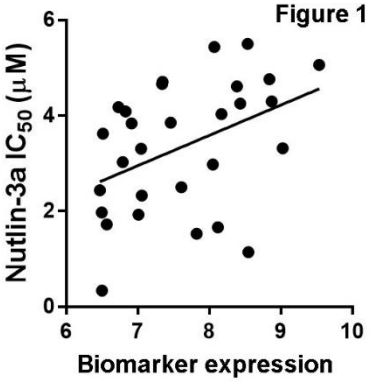


Figure 2

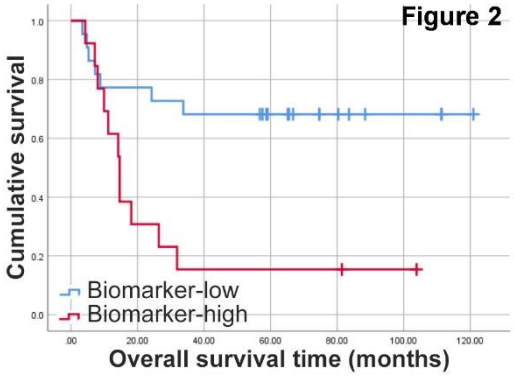
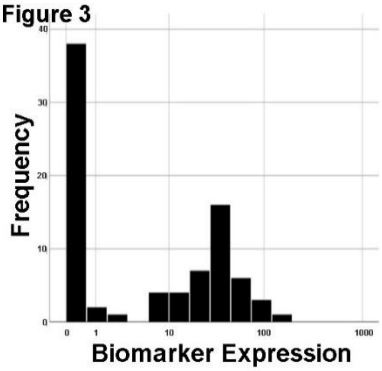


Figure 3



DEVELOPMENT STAGE

Biomarker and downstream targets successfully validated in 3 independent retrospective patient cohorts (*n* = 300).

COMMERCIAL OPPORTUNITY

This is an opportunity to acquire a novel patient stratification tool for the identification of patients most likely to respond to MDM2/4 inhibitor +/- cytarabine therapies. This biomarker assay represents a key new tool to developing personalised medicine and ensuring that each patient receives the best treatment.

We are currently seeking industry partners with the resources and capabilities for the rapid co-development and licensing of our assay

CONTACT

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