

Investigating novel drug combinations for acute myeloid leukaemia



Project title: Identifying Combination Therapies Targeting Apoptosis Pathways in Paediatric AML (CAuSAL study)

Lead researcher: Professor Ken Mills, Queens University Belfast

Project Stage: Complete (September 2020)

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ABOUT THE PROJECT

Leukaemia is the most commonly occurring cancer in children, with acute lymphoblastic leukaemia (ALL) accounting for 80% of leukaemia cases and acute myeloid leukaemia (AML) the remaining 20%.

Treatment and outcome for ALL patients has improved substantially over the years with overall survival now at 90%. Unfortunately, the outcome for paediatric AML is not as good with overall survival around 60%. Patients also have higher risk of relapse and of not responding to therapy and, when combined with the treatment side effects, these young people have a bleak outlook from diagnosis. Combination treatments, as opposed to single drug treatments, could make it more difficult for cancer cells to develop resistance.

The research team at Queen's University Belfast, led by Professor Ken Mills, will investigate the two new drug combinations that were identified through a unique method of combination screening (multiplex screening for interacting compounds in acute leukaemia - MuSICAL). They focused on drugs that would kill cells and screened all two drug combinations of 80 drugs using their MuSICAL method. This identified drugs which did not kill cells on their own but were very effective when combined.

The two combinations that the research team will test further are "ABT-737 plus Purvalanol A" and "SU9516 plus Pozotinib", found in a previous study. The researchers will find out how the drugs work together to see why the combination is more effective than each drug is alone. Finding a new drug combination will help AML patients whose relapse or whose first set of treatment does not go well and improve quality of life for patients who are on treatment by providing a therapy with less side effects. Professor Ken Mills hopes the drug combinations identified will be good enough to move forward into clinical trials and will eventually improve outcomes for paediatric AML patients.

RESULTS

This study found that combination of ABT-737 and Purvalanol A specifically can kill cells from AML subtypes with specific mutations.

The combination of ABT-737 and Purvalanol A was also tested on more types of paediatric AML cells, to see whether it had the potential to treat other AML subtypes. Interestingly, the data showed that this combination only works for the subtypes with specific mutations and none of the other types tested.

WHAT'S NEXT?

The research team plans to further validate these results and plan an extension of the project, initially using master's students to gain more data for a new grant application.



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