Study identifies kids with cancer at risk of developing lethal infections

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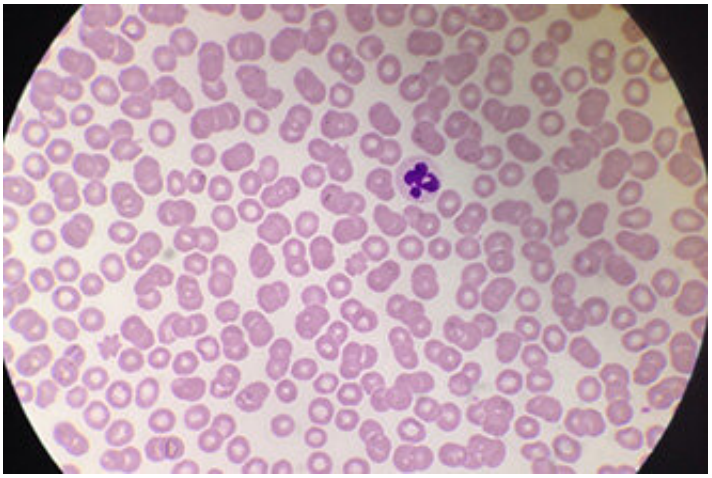

Febrile neutropenia occurs when patients contract a fever when their neutrophils are low. Credit: Walter and Eliza Hall Institute of Medical Research

New research published in *Clinical & Translational Immunology* has identified the child cancer patients at greatest risk of developing life-threatening infections, a crucial step towards the development of an early diagnostic test.

There is currently no clinical test to identify which children are likely to develop severe infections during febrile neutropenia (FN)—a condition common in chemotherapy patients—from those who are at low risk.

This WEHI-led study could prevent thousands of low-risk cancer

patients worldwide from undergoing unnecessary treatment and potentially disrupting their chemotherapy.

Children who are given chemotherapy have weakened immune systems, putting them at an elevated risk of contracting potentially life-threatening infections.

Any cancer patient that currently presents to hospital with FN is immediately given intravenous antibiotics to prevent possible infectious complications.

While less than a quarter of FN cases will become potentially life-threatening, there is currently no way to determine which patients will fall into this category.

A collaboration between WEHI, The Royal Children's Hospital, Murdoch Children's Research Institute and Peter MacCallum Cancer Center, has uncovered the first immune signatures that could be used to develop novel tests that can distinguish low to severe FN episodes.

The research, led by WEHI's Professor Marc Pellegrini and Dr. Marcel Doerflinger, is published in *Clinical & Translational Immunology*.

Improved interventions

Febrile neutropenia is a major cause of treatment disruption and unplanned hospitalization in childhood cancer patients. It occurs when patients contract a fever when their neutrophils (a type of white blood cell) are low.

About 50% of children treated with chemotherapy develop at least one FN episode. While only a fraction of patients with FN will have a life-threatening infection, all cases are treated as medical emergencies.

Dr. Marcel Doerflinger said FN and antibiotic resistance are critical problems during cancer therapy.

"We exacerbate both of these issues each time antibiotic treatment is administered unnecessarily," Dr. Doerflinger said.

Researchers hope their findings can prevent children from receiving unnecessary antibiotics, by helping clinicians optimize the use of the treatment for children most at risk of suffering severe complications.

"While febrile neutropenia is a serious concern for any immune-suppressed patient irrespective of age, there are some FDA-approved tests for adults that could prevent them from receiving this treatment without good cause," Dr. Doerflinger said.

"While such tests have not yet been translated to children, our findings help to bridge this crucial gap to ensure no harm is done to the quality of life of any child with cancer."

Landmark discovery

This is the first study worldwide that used cutting-edge gene sequencing tools to analyze the immune response during FN episodes in child cancer patients.

Leveraging WEHI's Next Generation Sequencing technology and skills from the Institute's bioinformatics team, researchers were able to compare the transcriptional profiles of blood cells from children with cancer and FN, to identify 24 genes that could be used to distinguish between mild and severe FN infections.

Professor Marc Pellegrini said it was the first time a research team had been able to do this type of analysis.

"Our landmark data shows that only patients with these specific immune signatures should be treated as FN medical emergencies," Professor Pellegrini said.

The key differences in the immune profiles of benign FN episodes and cases with severe infections were identified as cell death processes of immune cells, specific inflammatory responses and metabolic processes.

"This project was established to find potential biomarkers that could be tested for, as soon as children with cancer and FN present in hospital," Professor Pellegrini said. "This would enable clinicians to determine a patient's infection severity and most importantly, to customize treatment.

"Our findings are a crucial step towards developing this important tool that could spare thousands of children around the world from unnecessary treatment."

More information: Gabrielle M Haeusler et al, Blood transcriptomics identifies immune signatures indicative of infectious complications in childhood cancer patients with febrile neutropenia, *Clinical & Translational Immunology* (2022). DOI: 10.1002/cti2.1383

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