

Diagnostic biomarker for acute myeloid leukemia (AML) M5 subtype



Our data indicate that elevated expression of the interleukin-27 receptor (IL27R) in peripheral blood or bone marrow cells acts as a diagnostic marker for the AML M5 subtype. This is consistent with the finding that aberrant expression of wild-type IL27R can induce transformation of hematopoietic cells. The M5 subtype is a prognostically unfavorable disease that often presents with non-specific symptoms, causing difficult diagnosis and delayed treatment. In contrast to the current method of diagnosis of AML M5 that requires an invasive bone marrow biopsy, our test can be performed as an addition to the current flow-cytometry protocol that is used to differentiate AMLs from other leukemias such as ALL. Our assay could therefore use peripheral blood leading to a faster and less invasive diagnosis than a bone marrow biopsy.

COMMERCIAL OPPORTUNITY

- There are approximately 10,500 new AML cases in the US each year, of which approximately 10% belong to the M5 subtype. M5 is a prognostically unfavorable disease calling for prompt aggressive treatment (either intense chemotherapy or a bone marrow transplant). However, because M5 often presents with non-specific symptoms, patients may undergo several rounds of diagnostic tests (including expensive imaging scans) before AML M5 is diagnosed.
- Bone marrow biopsy remains the “gold standard” of AML diagnosis, including M5. It is invasive, painful, and can cause serious complications such as infections and bleeding. In contrast, our test can be added to routine bloodwork, in order to diagnose the M5 subtype quickly and accurately, and potentially spare the M5 subtype patients a painful biopsy. Alternatively, it could be used on the bone marrow aspirate to confirm the AML M5 diagnosis.
- Our test can be performed by either flow cytometry or immuno-assay, using a small sample of peripheral blood and/or bone marrow. Both techniques are routinely used in clinics to diagnose AML. Therefore, our M5 test can be added to a panel of tests commonly used to diagnose AML. This will not disturb the standard of care diagnostic procedures, making the implementation of our test feasible and relatively inexpensive.

TECHNOLOGY

To identify oncogenes involved in AML, 32D myeloid progenitor cells that depend on IL-3 for growth and viability were transfected with cDNAs representing the genes expressed in an AML FAB subtype M5b monocytic leukemia. Two days after infection using retroviral vectors, 32D/Bcl2 cells were plated in medium lacking IL-3 to identify IL-3-independent transformants. A cDNA encoding the WT IL-27R alpha gene was isolated from one transformant. To determine whether this gene was commonly expressed in AML patients, flow cytometry was used to detect IL-27R on the cell surface of AML cells. Eight of 13 AML bone marrow samples tested had 2.5- to 10-fold more cells expressing IL-27R (ranging from 0.33% to 84.6%) than the average observed in normal bone marrow cells (ranging from 6.3% to 12.8%) with the five highest IL-27R-expressing bone marrow samples being the M5 subtype.

PUBLICATION/PATENT

- Pradhan A, Lambert QT, Reuther GW (2007). PNAS 104(47):18502-7
- US Patent US8367344 issued on behalf of GW Reuther.

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LICENSING OPPORTUNITY

