### All you need to know about large immature cells (LIC) and atypical lymphocytes (ALY)

The HumaCount 5D is a 5-part hematology analyzer that determines 29 parameters on human whole blood samples. Besides the differentiation of white blood cells in lymphocytes, monocytes, neutrophils, eosinophils and basophils, the system provides all common erythrocyte and platelet parameters. As an additional feature, the HumaCount 5D determines two research parameters: Large immature cells (LIC) and atypical lymphocytes (ALY).



#### What are large immature cells?

Large immature cells are precursors of the mature granulocytes<sup>\*</sup>. Under normal conditions, granulocytes develop in the bone marrow before being released into the peripheral blood. The appearance of immature cells in the peripheral blood of a healthy adult indicates a response to an infection, inflammation or any other stimuli of the bone marrow like for example a hematological malignancy.<sup>1</sup>

#### What are atypical lymphocytes?

Atypical lymphocytes are lymphocytes that have been activated to respond to a viral infection or in certain cases a bacterial or parasitic infection. The cells are larger than naive lymphocytes. Atypical lymphocytes have increased in size due to activation by an antigen, which in turn triggers increased synthesis of mRNA and protein.

\*Other manufacturers may call the large immature cells "IG" for "immature granulocyte".



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#### What do large immature cells indicate?

An increased immature cell count may indicate the severity of the early innate immune response.

Therefore, the parameter is especially relevant for patients who are susceptible to infections e.g. due to immune suppression. In addition to patients with general infections and inflammations, the parameter becomes important for patients on intensive care units, patients undergoing chemotherapy and HIV-patients.

A high number of LICs is often described as a 'left-shifted' leukogram, with more banded cells and metamyelocytes present while segmented neutrophils are already depleted in the blood due to the high consumption.

The LIC count alone cannot predict a certain disease type like infection or malignancy. However, it supports diagnosis and prediction together with other parameters such as cytokines, interleukins and CRP.

The LIC count of pediatric patients, especially premature neonates or neonates younger than seven days, has to be taken with care due to their immature immune systems and the greater number of immature cells in the circulating blood.

The HumaCount 5D will show a flag as well as an absolute number and percentage for the LIC parameter. However, as this is a research parameter, the user should validate the parameter using additional methods.



#### What do atypical lymphocytes indicate?

ALY in the peripheral blood are always an alarm signal. They are seen in the blood of patients suffering from acute lymphoblastic leukemia (ALL); viral disease such as cytomegalovirus, Epstein Barr Virus, hepatitis C; bacterial infections such as toxoplasmosis; exposure to radiation; drug and immunization reactions; and other immune responses.<sup>2,3</sup>

Like LIC, ALY is a research parameter on the HumaCount 5D. The analyzer will show a flag and give absolute numbers as well as percentages, but the parameter needs to be validated by other means.

#### Can large immature cells and atypical lymphocytes be reported as blast cells?

Both of the cell types, LIC and ALY, can be considered as blast cells. Blasts are defined as precursors to the mature, circulating blood cells such as neutrophils, monocytes, lymphocytes and erythrocytes. As mentioned before these circulating blasts can be seen with severe infections, medications (e.g. granulocyte colony stimulating factor), bone marrow replacing processes and hematopoietic neoplasms. The LIC are of myeloid origin, whereas the ALY are lymphocytic.



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#### Normal values of atypical lymphocytes and large immature cells

The default reference ranges which are stored in the HumaCount5D software are shown in the table below:

Parameter	Lower level	Upper level	Unit	
ALY #	0	0.2	10³/µl	Table 1: reference ranges <sup>4,5</sup>
ALY %	0	2.0	%	
LIC #	0	0.2	10³/µl	•
LIC %	0	2.5	%	•

However, these default ranges need to be treated with caution, because the "normal" values can be different depending on the population, age, gender, etc. As all reference ranges which are stored in the HC5D software, also these ones can be edited by the user.

#### Where are blast cells located in the HumaCount 5D scattergram?



The figure on the left shows a schematic view of where to find the ALY and LIC populations in the scattergram. Atypical lymphocytes (ALY) are bigger than lymphocytes but smaller than monocytes. Therefore, this population can be found between LYM and MON. The size of large immature cells (LIC) is much bigger compared to NEU, so this population gives a much stronger LS signal and can be clearly discriminated from the other cell populations.

5-part diff and LIC, ALY parameters

#### References

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