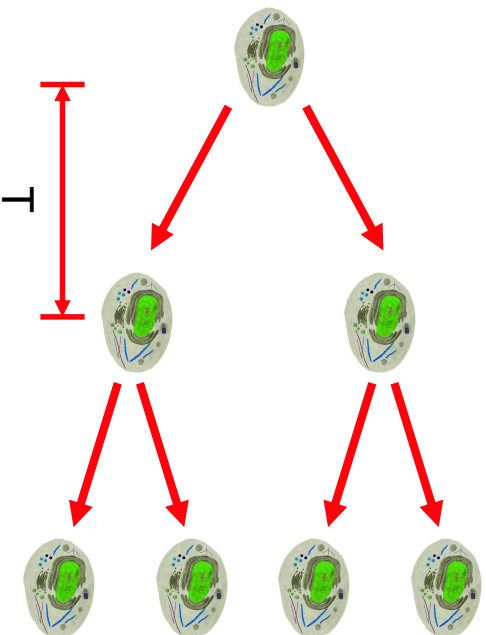


## Cell duplication time (cell cycle time)



n	number of cells	time
0	1	0
1	2	1 T
2	4	2 T
3	8	3 T
4	16	4 T
5	32	5 T
6	64	6 T

1

## Exponential growth:

$$n [(m + 1)T] = 2 n (mT)$$

new population twice as large as the old one

$$n (mT) = 2^m \times n(0)$$

going back to the initial population the increase is exponential

$$n(t) = 2^{t/T} \times n(0)$$

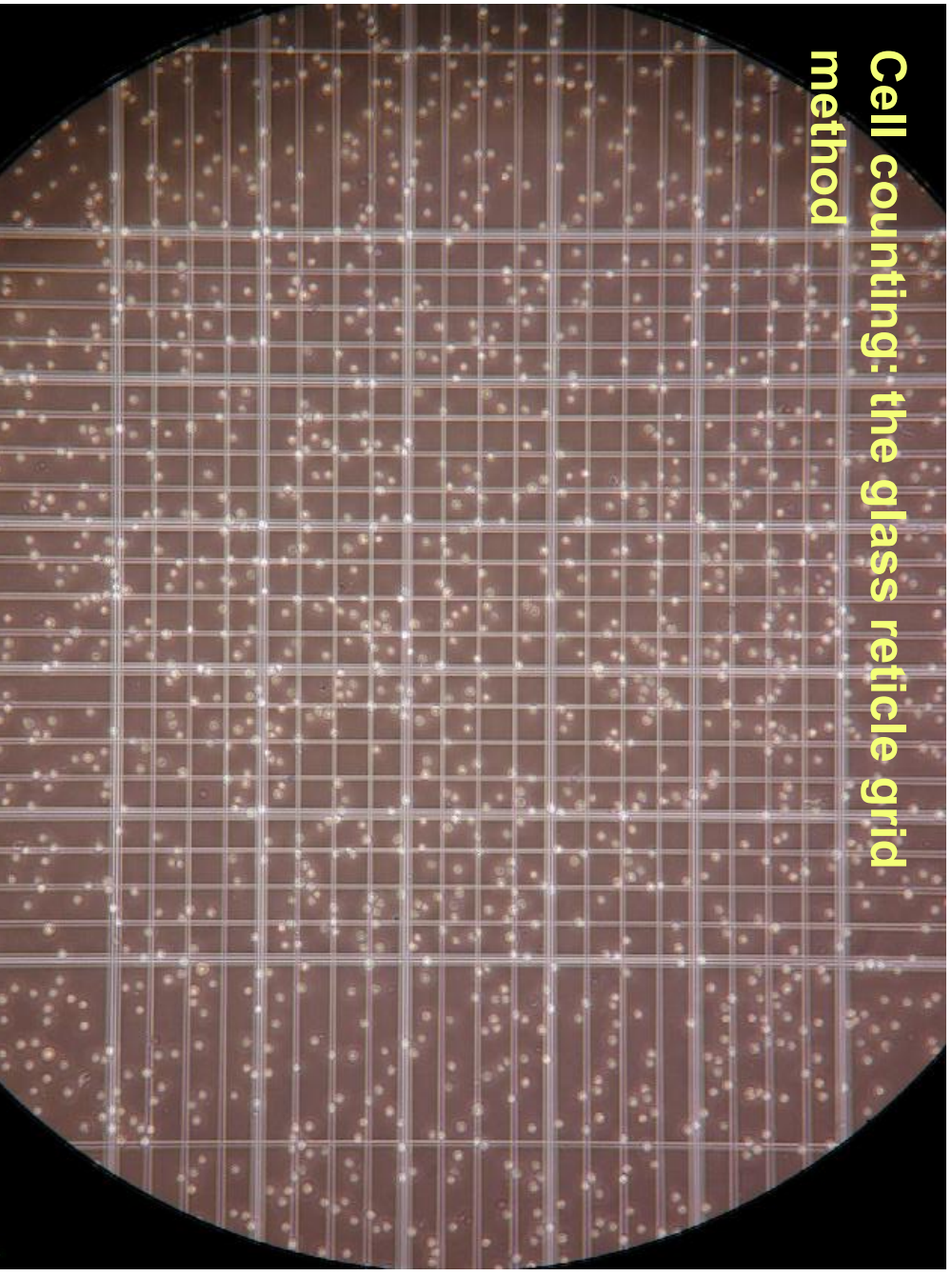
by writing  $m = t/T$  we introduce time

$$\ln n(t) = \ln n(0) + \frac{t}{T} \ln 2$$

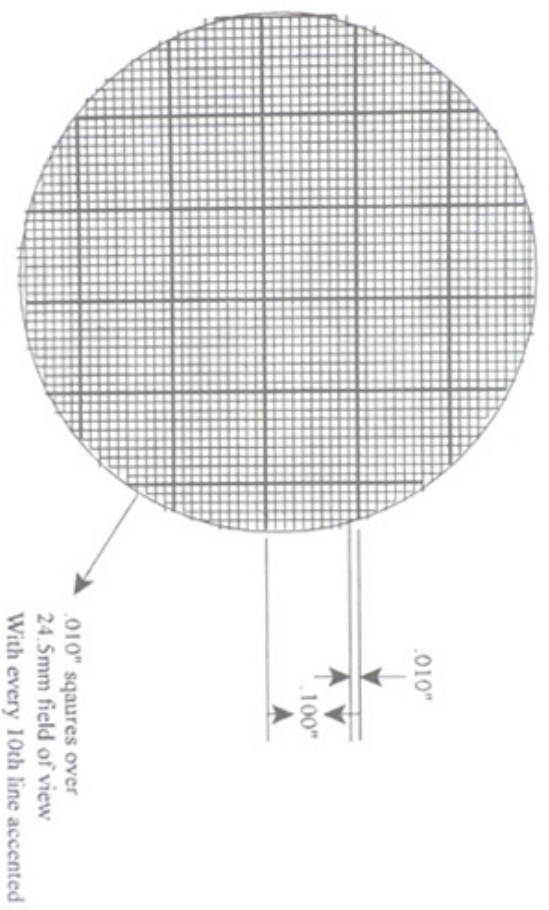
the same formula can be written differently, and we see that the log of the population size is a linear function of time

2

## Cell counting: the glass reticle grid method



A commercial reticle grid



## Statistics:

(N = number of squares of the reticle grid)

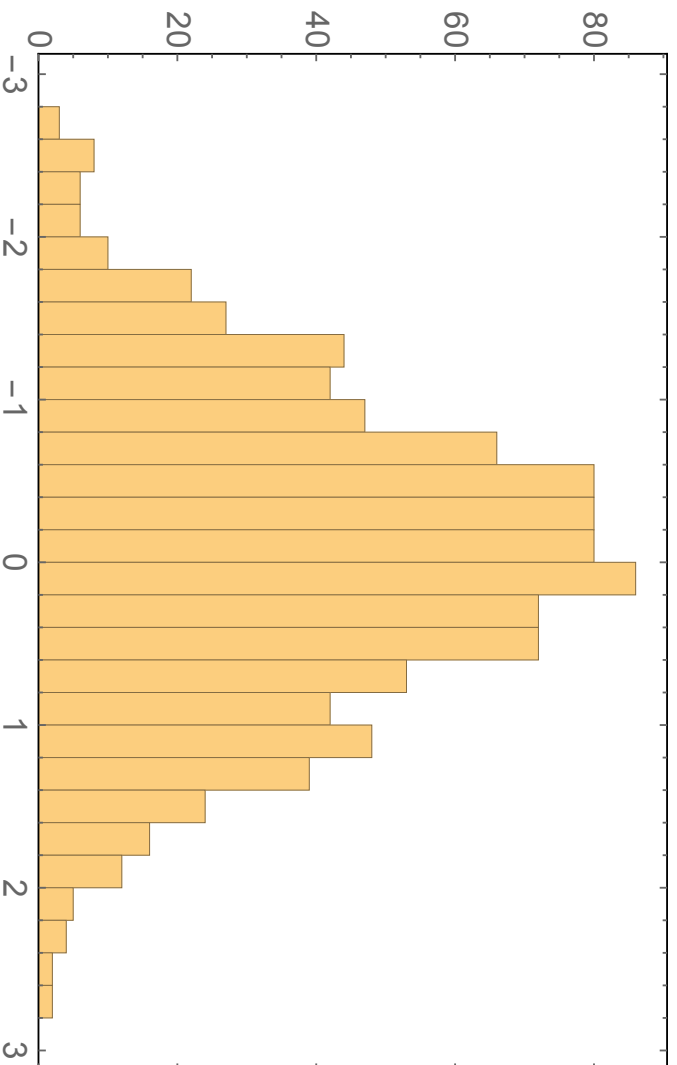
**population mean:** 
$$\langle n \rangle = \frac{1}{N} \sum_{k \in \{\text{squares}\}} n_k$$

**population variance:** 
$$\text{var } n = \frac{1}{N-1} \sum_{k \in \{\text{squares}\}} (n_k - \langle n \rangle)^2$$

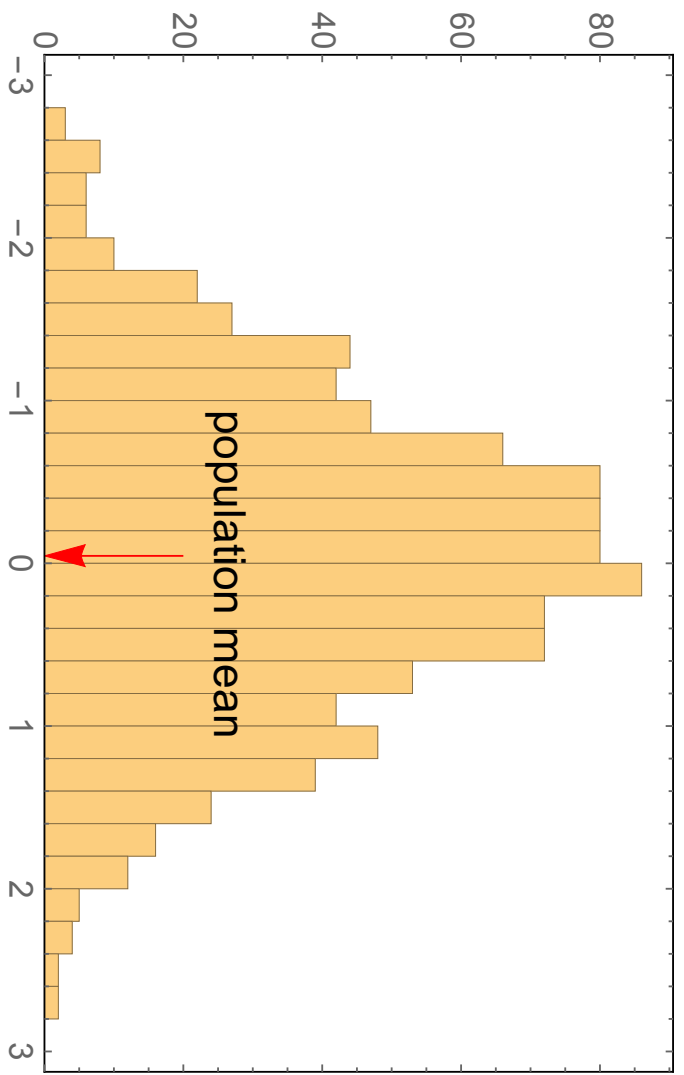
**standard deviation:** 
$$\sigma_n = \sqrt{\text{var } n}$$

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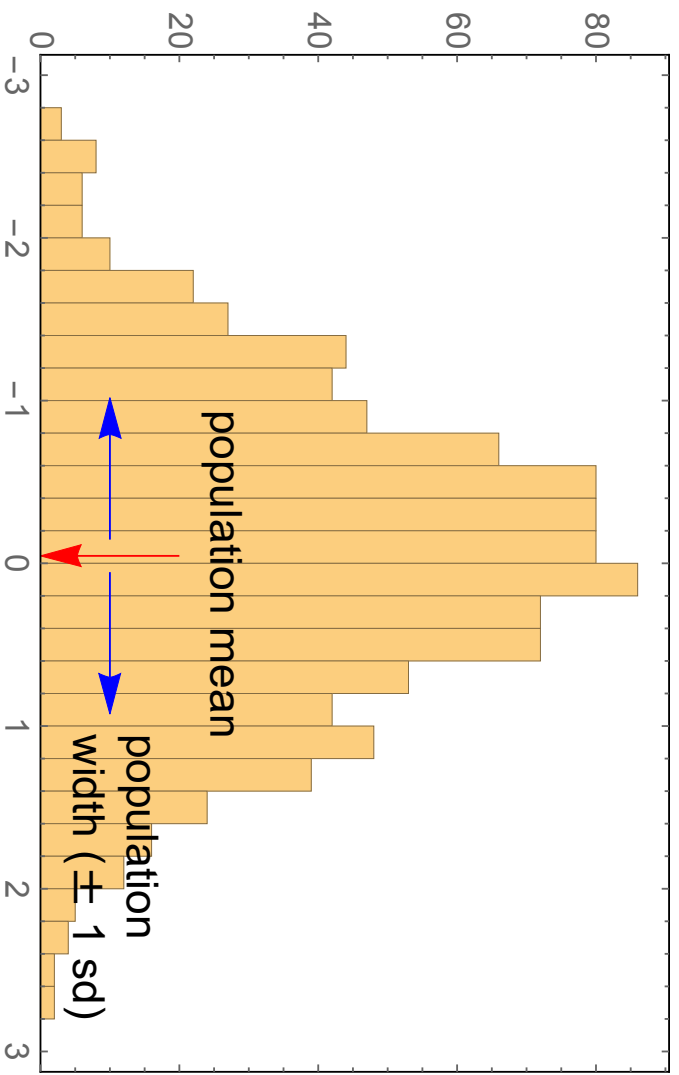
Example: 1. Histogram of 1000 measurements  $x_k$  (binsize = 0.2)



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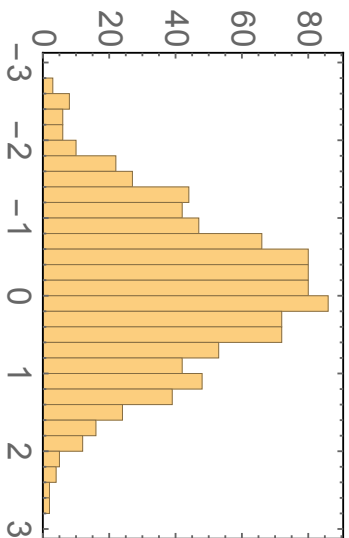
7



8

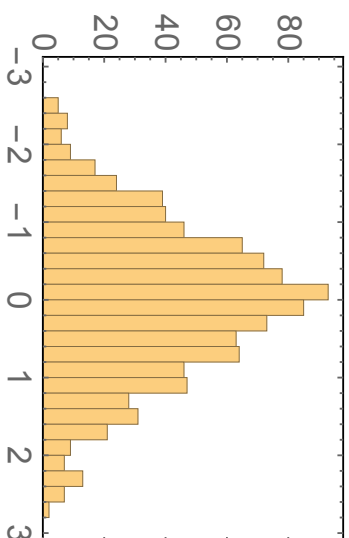
Mean : -0.0457642

Standard Deviation : 0.972646



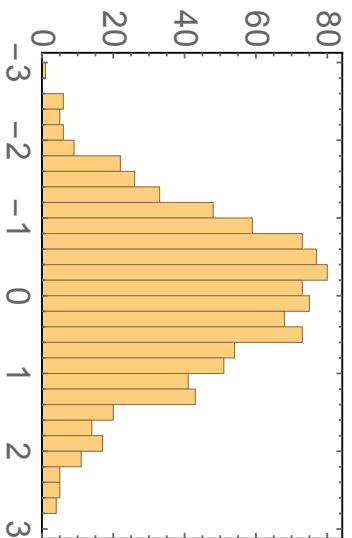
Mean : 0.0201908

Standard Deviation : 0.993215



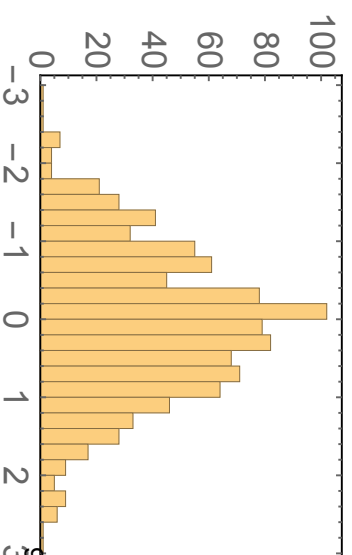
Mean : -0.0112601

Standard Deviation : 0.992668



Mean : 0.0542286

Standard Deviation : 0.951379



## Variance of the population mean

$$\text{var}(\alpha n) = \alpha^2 \text{var } n$$

$$\text{var} \sum_k n_k = \sum_k \text{var } n_k$$

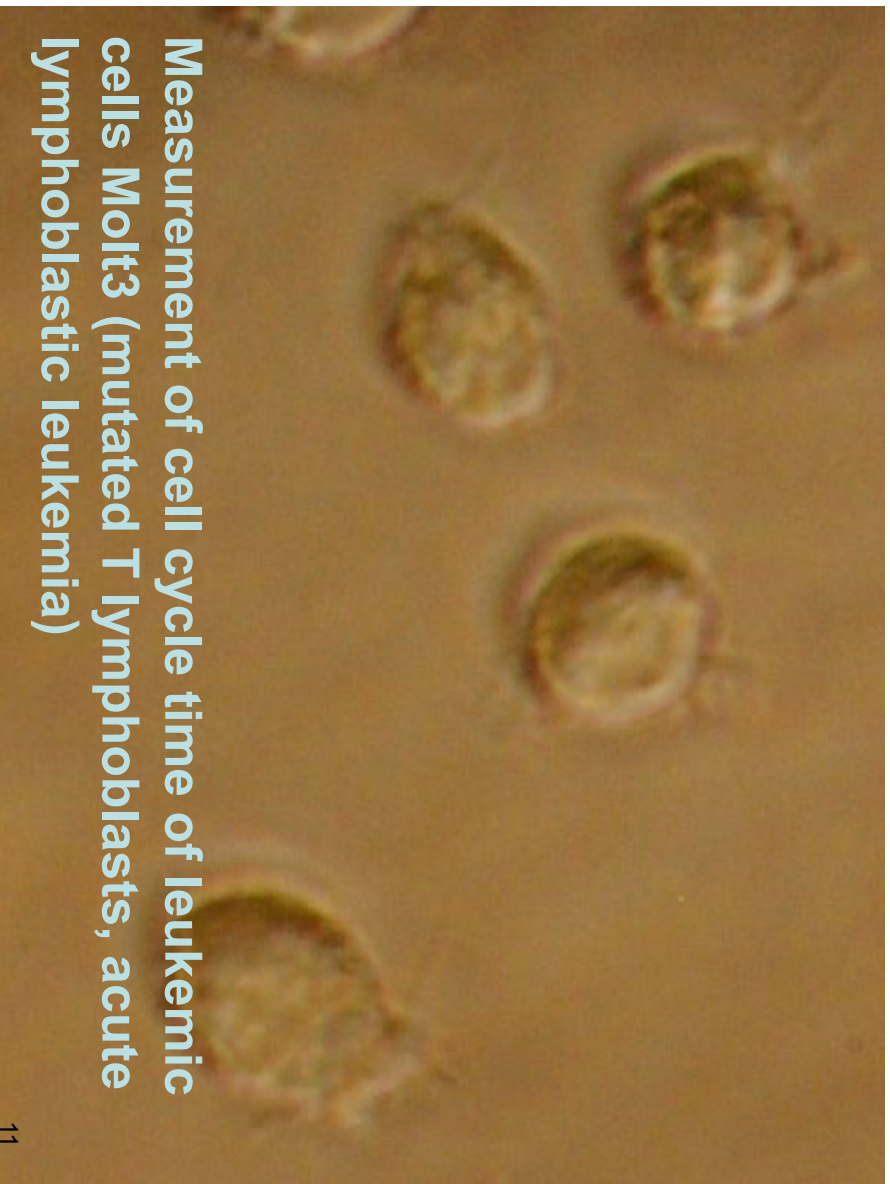
$$\text{var } n_k = \sigma^2$$

$$\langle n \rangle = \frac{1}{N} \sum_{k \in \{\text{squares}\}} n_k$$

- multiplication by a scalar
- variance of a sum of **independent** variables
- all measurements have the same variance
- population mean has **both** a scaling constant **and** is a sum of independent variables

$$\text{var} \langle n \rangle = \frac{1}{N(N-1)} \sum_{k \in \{\text{squares}\}} (n_k - \langle n \rangle)^2$$

As a result, this is the variance of the population mean



## Measurement of cell cycle time of leukemic cells Molt3 (mutated T lymphoblasts, acute lymphoblastic leukemia)

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### **Leukemia**

Leukemia is a group of blood cancers that usually begin in the bone marrow and result in high numbers of abnormal blood cells. These blood cells are not fully developed and are called blasts or leukemia cells.

Symptoms may include bleeding and bruising, bone pain, fatigue, fever, and an increased risk of infections. These symptoms occur due to a lack of normal blood cells. Diagnosis is typically made by blood tests or bone marrow biopsy.

The exact cause of leukemia is unknown. A combination of genetic factors and environmental (non-inherited) factors are believed to play a role. Risk factors include smoking, ionizing radiation, petrochemicals (such as benzene), prior chemotherapy, and Down syndrome. People with a family history of leukemia are also at higher risk.

There are four main types of leukemia—acute lymphoblastic leukemia (ALL), acute myeloid leukemia (AML), chronic lymphocytic leukemia (CLL) and chronic myeloid leukemia (CML) – as well as a number of less common types.

Leukemias and lymphomas both belong to a broader group of tumors that affect the blood, bone marrow, and lymphoid system, known as tumors of the hematopoietic and lymphoid tissues.

Treatment may involve some combination of chemotherapy, radiation therapy, targeted therapy, and bone marrow transplant, in addition to supportive care and palliative care as needed. Certain types of leukemia may be managed with watchful waiting.

(Adapted from Wikipedia)

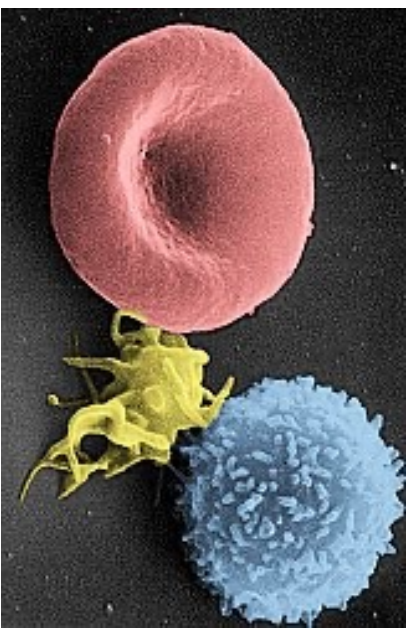


T cells are one of the important types of white blood cells of the immune system and play a central role in the adaptive immune response. T cells can be distinguished from other lymphocytes by the presence of a T-cell receptor (TCR) on their cell surface.

T cells are born from hematopoietic stem cells, found in the bone marrow. Developing T cells then migrate to the thymus gland to develop (or mature). T cells derive their name from the thymus. After migration to the thymus, the precursor cells mature into several distinct types of T cells. T cell differentiation also continues after they have left the thymus. Groups of specific, differentiated T cell subtypes have a variety of important functions in controlling and shaping the immune response.

CD8+ T cells, also known as "killer T cells", are cytotoxic – this means that they are able to directly kill virus-infected cells, as well as cancer cells.

(Adapted from Wikipedia)



Scanning electron micrograph of a red blood cell (left), a platelet (center), and a T lymphocyte (right); colorized

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*Blood*, Vol 72, No 5 (November), 1988: pp 1755-1760

## **Immunophenotypic and Cytogenetic Analysis of Molt-3 and Molt-4: Human T-Lymphoid Cell Lines With Rearrangement of Chromosome 7**

By James M. Greenberg, Rogelio Gonzalez-Sarmiento, Diane C. Arthur, Christopher W. Wilkowski, Barbara J. Streifel, and John H. Kersey

...

The Molt-3 and Molt-4 cell lines were established by Minowada et al in 1971 from the peripheral blood of a 19-year-old man with acute lymphoblastic leukemia. Both cell lines were originally described as having lymphoid morphology with phenotypic characteristics of T cells.

...

Cytogenetic studies of Molt-4 performed by Huang et al. shortly after establishment of the cell line in 1971 revealed a diploid karyotype that converted to a tetraploid karyotype after 11 months in culture. Thus, the tetraploidy that we describe now has been a feature of Molt-4 (and presumably Molt-3) for many years, but it was probably not a feature of these cells *in vivo*. Tetraploid karyotypes have been described in acute leukemia, presumably secondary to DNA replication without cell division.

...

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