

Researchers discover genetic origins of myelodysplastic syndrome using stem cells

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Induced pluripotent stem cells (iPSCs)—adult cells reprogrammed back to an embryonic stem cell-like state—may better model the genetic contributions to each patient's particular disease. In a process called cellular reprogramming, researchers at Icahn School of Medicine at Mount Sinai have taken mature blood cells from patients with myelodysplastic syndrome (MDS) and reprogrammed them back into iPSCs to study the genetic origins of this rare blood cancer. The results appear in an upcoming issue of *Nature Biotechnology*.

In MDS, genetic mutations in the bone marrow stem cell cause the number and quality of blood-forming cells to decline irreversibly, further impairing blood production. Patients with MDS can develop severe anemia and in some cases leukemia also known as AML. But which genetic mutations are the critical ones causing this disease?

In this study, researchers took cells from patients with blood cancer MDS and turned them into [stem cells](#) to study the deletions of human chromosome 7 often associated with this disease.

"With this approach, we were able to pinpoint a region on chromosome 7 that is critical and were able to identify candidate genes residing there that may cause this disease," said lead researcher Eirini Papapetrou, MD, PhD, Department of Oncological Sciences, Icahn School of Medicine at Mount Sinai.

Chromosomal deletions are difficult to study with existing tools because

they contain a large number of genes, making it hard to pinpoint the critical ones causing cancer. Chromosome 7 deletion is a characteristic cellular abnormality in MDS and is well-recognized for decades as a marker of unfavorable prognosis. However, the role of this deletion in the development of the disease remained unclear going into this study.

Understanding the role of specific chromosomal deletions in cancers requires determining if a deletion has observable consequences as well as identifying which specific genetic elements are critically lost.

Researchers used [cellular reprogramming](#) and genome engineering to dissect the loss of chromosome 7. The methods used in this study for engineering deletions can enable studies of the consequences of alterations in genes in human cells.

"Genetic engineering of human stem cells has not been used for disease-associated genomic deletions," said Dr. Papapetrou. "This work sheds new light on how blood cancer develops and also provides a new approach that can be used to study chromosomal deletions associated with a variety of human cancers, neurological and developmental diseases."

Reprogramming MDS cells could provide a powerful tool to dissect the architecture and evolution of this disease and to link the genetic make-up of MDS cells to characteristics and traits of these cells. Further dissecting the MDS stem cells at the molecular level could provide insights into the origins and development of MDS and other [blood cancers](#). Moreover, this work could provide a platform to test and discover new treatments for these diseases.

More information: Functional analysis of a chromosomal deletion associated with myelodysplastic syndromes using isogenic human induced pluripotent stem cells, [DOI: 10.1038/nbt.3178](https://doi.org/10.1038/nbt.3178)

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