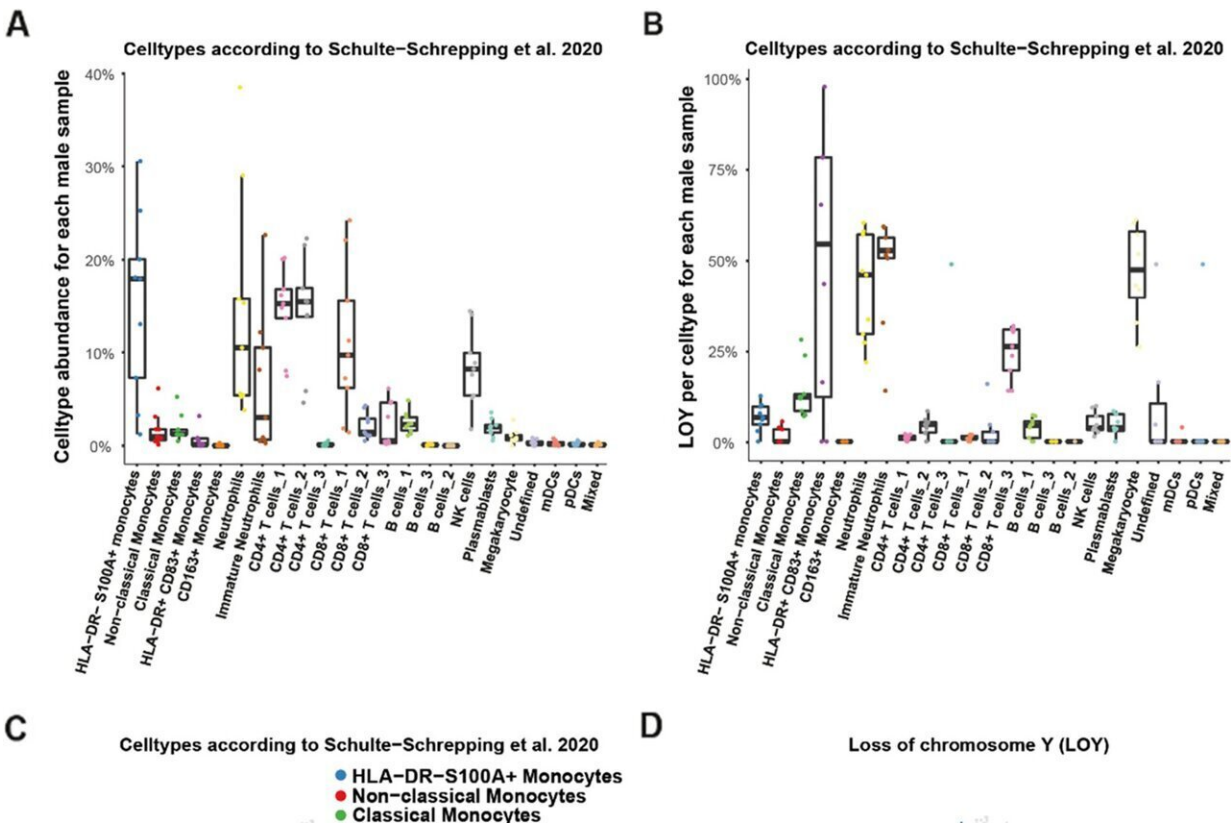


Y chromosome loss may be linked to men's increased risk of severe COVID-19

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Distribution of cell types and cells with loss of chromosome Y (LOY) in PBMCs from critically ill patients with COVID-19. The dataset comes from Schulte-Schrepping et al. 2020 [19] and we used cell type annotation reported therein. Nine PBMCs samples from six male patients with WHO score ≥ 5 were used for calculations. A Proportion of cell types in PBMCs; each data point represents a single sample. B Proportion of cells with LOY per cell type and per sample; each data point represents a single sample. C UMAP projection of scRNA-seq profiles, selected cell types are colored. D UMAP visualization of scRNA-seq

profiles colored according to LOY status. Cells classified as LOY cells had no detectable expression from chromosome Y. Credit: *Genome Medicine* (2022). DOI: 10.1186/s13073-022-01144-5

Men are at an increased risk of a severe bout of COVID-19 compared to women. Researchers at Uppsala University have now shown that this may be due to loss of the Y chromosome in part of their white blood cells. The findings could eventually be used to assess the risk of developing severe COVID-19 and perhaps to improve treatment.

A common genetic change in men is loss of the Y chromosome (LOY) in a part of the white blood cells. Interestingly, this change is more common with advancing age.

During the COVID-19 pandemic, it became quickly apparent that men were more severely affected by the disease. Up to 75% of patients in intensive care units have been men and the proportion of men who have died is also higher compared to women. In the current study, the researchers have discovered a connection between LOY and the risk of severe COVID-19.

"We studied [blood samples](#) taken from over 200 [male patients](#) in intensive care units between the beginning of 2020 and the summer of 2021. Our analyses showed that LOY was linked both to the severity of the disease, based on the WHO grading, and to the risk of dying," says Bożena Bruhn-Olszewska, researcher at Uppsala University.

Several findings in the study support that LOY is important for the development of severe COVID-19. A higher proportion of LOY could be linked to impaired lung function, e.g. lower oxygenation. Complications in the form of blood clots also showed an association with

a higher percentage of LOY in specific types of white blood cells. In addition, it was noted that the higher proportion of cells with LOY was transient.

"We had the opportunity to analyze samples taken from some of the patients three to six months after they were discharged from the [intensive care unit](#). In these samples, the proportion of cells with LOY had drastically decreased. As far as we know, this is the first time anyone has shown that LOY has dynamic properties linked to an acute infectious disease," explains Hanna Davies, researcher at Uppsala University.

The researchers believe that LOY could be used as a biomarker to predict which patients are at risk of severe disease development from COVID-19.

"Our results contribute to a better understanding of the importance that LOY has for susceptibility to the disease, especially in relation to the functioning of the immune system. We also believe that the new knowledge may be relevant to other common viral infections that are more serious for men than for women," says Jan Dumanski, Professor at Uppsala University who led the study.

The research is published in the journal *Genome Medicine*.

More information: Bożena Bruhn-Olszewska et al, Loss of Y in leukocytes as a risk factor for critical COVID-19 in men, *Genome Medicine* (2022). [DOI: 10.1186/s13073-022-01144-5](https://doi.org/10.1186/s13073-022-01144-5)

Provided by Uppsala University

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