Researchers develop novel platform to improve immunotherapy

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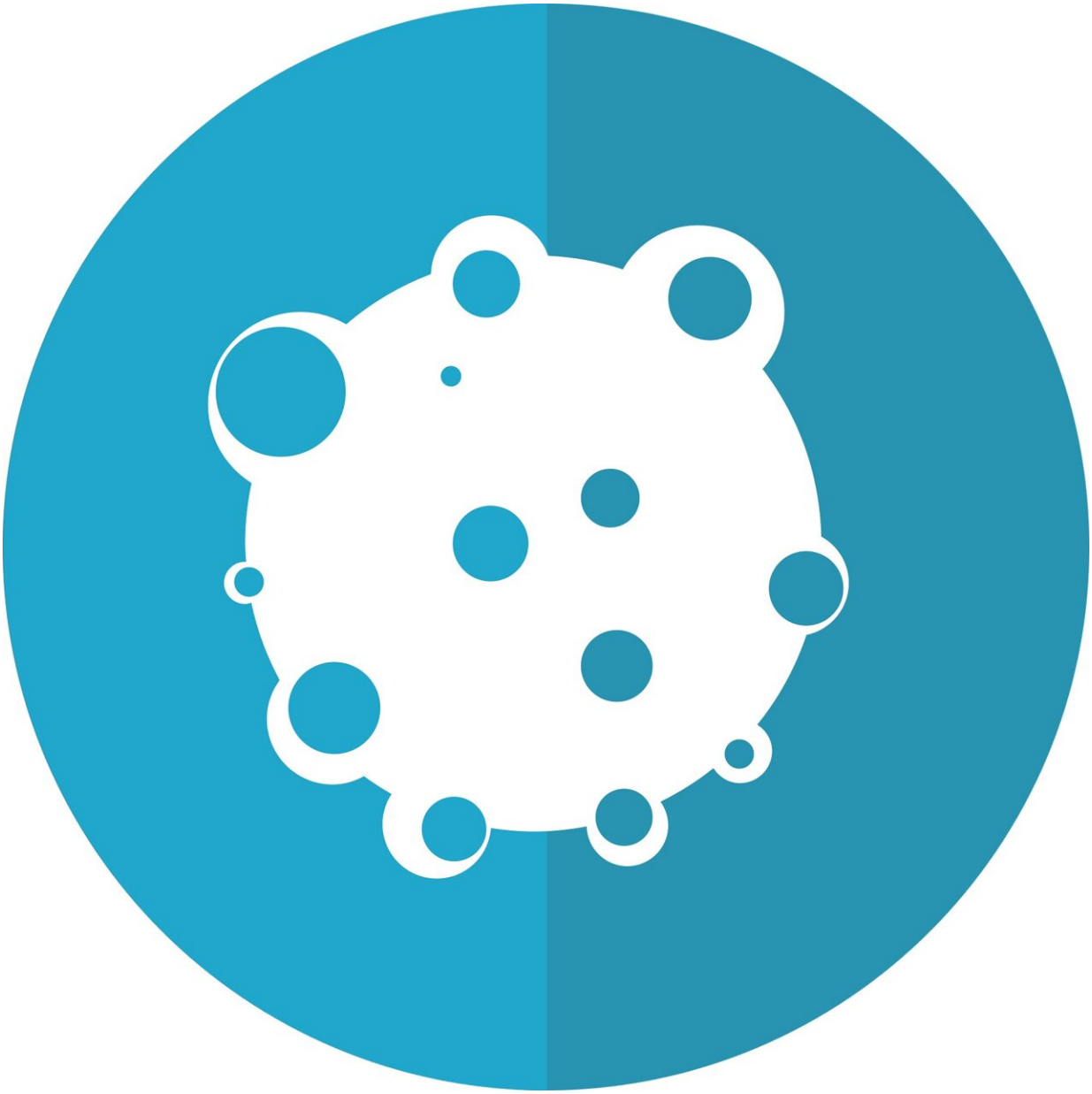

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Recent advances in immunotherapy for cancer have stimulated a plethora of studies aimed at developing T cells (white blood cells) and Natural Killer (NK) cells (immune cells with enzymes that can kill tumor cells or cells infected with a virus) in-vitro from pluripotent stem cells—cells that are able to self-renew by dividing and developing into the three primary groups of cells that make up a human body.

Now, researchers from Boston University Chobanian & Avedisian School of Medicine and Boston Medical Center have discovered a novel pathway based on Notch stimulation (a pathway involved in cell fate decisions, proliferation and death) very early during the in-vitro differentiation that robustly support the emergence of T and NK cells from human induced Pluripotent Stem Cells (iPSC).

"A robust method of producing mature T cells from iPSCs is needed to realize their therapeutic potential," says corresponding author Gustavo Mostoslavsky, MD, Ph.D., associate professor of medicine & microbiology. NOTCH1 is known to be required for the production of hematopoietic progenitor cells (an intermediate cell type in blood cell development) with T cell potential in vivo. "We have identify a critical window when Notch activation robustly improves access to definitive intermediate cell type in blood cell development (hematopoietic progenitors) with T/NK cell lineage potential."

According to the researchers, current practices for immunotherapy are prohibitively expensive and are accompanied by serious adverse events. "The establishment of platforms that will make this process safer, simpler and cheaper will have tremendous implications on public health and in general on the way these therapies are applied in the clinic," adds

Mostoslavsky who also is co-director of the BU/BMC Center for Regenerative Medicine (CReM).

The researchers believe a novel platform allowing universal off-the-shelf T and NK cell access has enormous potential for future immunotherapies targeting a broad range of diseases, including cancer, autoimmune diseases such as rheumatoid arthritis and lupus, as well as immunodeficiencies.

These findings appear online in the journal *Stem Cell Reports*.

More information: Gustavo Mostoslavsky, Notch activation during early mesoderm induction modulates emergence of the T/NK cell lineage from human iPSCs., *Stem Cell Reports* (2022). DOI: 10.1016/j.stemcr.2022.10.007. www.cell.com/stem-cell-reports … 2213-6711(22)00503-3

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