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Vitamin C may boost effectiveness of acute myeloid leukemia treatment

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A simple adjustment to patients' therapeutic regimen may improve the effectiveness of the standard epigenetic treatment for myeloid dysplastic syndrome (MDS) and acute myeloid leukemia (AML).

New findings published today in the *Proceedings of the National Academy of Sciences* showed in lab studies that supplementing an epigenetic cancer drug called decitabine with vitamin C enhanced the drug's ability to impede cancer cell growth and trigger cellular self-destruction in cancer cell lines. A pilot clinical trial based on this work is ongoing in adult patients with MDS or AML at Rigshospitalet in Copenhagen, Denmark. It combines a similar drug called azacitidine—the standard of care therapy—with vitamin C. Many cancer patients are deficient in vitamin C; the proposed approach seeks to correct this deficiency rather than overload patients with the vitamin.

"If the pilot trial is successful, we plan to pursue a larger trial to explore this strategy's potential as a straightforward and cost-effective way to improve the existing therapy for AML and MDS," said Peter Jones, Ph.D., D.Sc., co-senior author of the *PNAS* study, chief scientific officer at Van Andel Research Institute (VARI) and co-leader of the Van Andel Research Institute-Stand Up To Cancer (VARI-SU2C) Epigenetics Dream Team. "At the same time, we must urge patience and caution. Only a clinical trial that combines azacitidine with the blinded addition of either vitamin C or a placebo will give the true answer as to whether or not vitamin C increases the efficacy of azacitidine in patients. We must emphasize that our trial is limited to a certain subset of patients

with MDS or AML on a specific therapeutic regimen. We do not have evidence that this approach is appropriate for other cancers or chemotherapies."

The proposed strategy reflects a continuing move toward combination therapies, particularly when it comes to epigenetic approaches, which target the mechanisms that control whether genes are switched "on" or "off." In cancer, these switches inappropriately activate or silence important genes, such as those that regulate cell growth and life cycle, ultimately leading to tumors. Epigenetic therapies are thought to work in two ways to fix these errors in cancer cells—by correcting the "position" of the gene switches and by making the cell appear as though it's infected by a virus, triggering the immune system.

The trial is led by Kirsten Grønbæk, M.D., DMSc., chief hematologist and professor at University of Copenhagen's Rigshospitalet and member of the VARI-SU2C Epigenetics Dream Team, which is supporting the trial and associated research. It will include 20 patients; preliminary results are expected by spring or summer 2017.

"This type of combination therapy is promising but more work is needed to determine its safety and efficacy," Grønbæk said. "It is truly exciting to consider that there could be a simple and elegant approach to help patients fight MDS and AML. However, as a physician, I strongly urge patients to wait for the results of the clinical trial and to discuss all dietary and supplemental changes with their doctors."

An estimated 13,000 people in the U.S. are diagnosed with MDS annually and about 20,000 are diagnosed with AML. Currently, only about half of patients with MDS and AML respond to the epigenetic therapy alone.

More information: Vitamin C increases viral mimicry induced by

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5-aza-2′-deoxycytidine, *Proceedings of the National Academy of Sciences*, www.pnas.org/cgi/doi/10.1073/pnas.1612262113

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