

More accurate markers identified for detecting response to epigenetic drugs for myelodysplastic syndromes

April 8 2013

Researchers have identified and validated two DNA methylation markers that could help physicians to more accurately determine a patient's response to epigenetic drugs for treatment of myelodysplastic syndromes (MDS), according to Xiaojing Yang, Ph.D., a postdoctoral fellow at the University of Southern California, Los Angeles, who presented the data at the AACR Annual Meeting 2013, held in Washington, D.C., April 6-10.

"The current feedback from physicians is that they cannot tell if a patient is really getting the epigenetic drug they are being treated with or not, which makes it difficult for them to decide whether to stop treatment or increase the dosage of the drug," said Yang. "This pushed us to think, why? Why didn't the current marker work and should we try to seek a better one?"

These drugs, called [DNA methyltransferase](#) inhibitors (DNMTi), work by turning on genes that suppress [cancer development](#), according to Yang. In patients with MDS, these genes are often silenced by the attachment of chemicals called methyl groups to the [DNA backbone](#) of the gene (an epigenetic modification made through a process called methylation), and DNMTi prevent methyl group attachment to DNA.

Currently, measuring methylation changes in [DNA sequences](#) known as LINE-1 elements is widely used as a predictor of whether or not DNMTi

are working, but recent research has found that LINE-1 remethylation after a DNMTi is withdrawn occurs faster than in other regions. This implies that LINE-1 methylation changes may not reflect overall demethylation effects of DNMTi, according to Yang.

Yang and colleagues sought to find improved markers of [DNA methylation](#) status. Using the Infinium DNA methylation platform, they assessed the methylation profile of 27,000 [genomic regions](#). The team tested this methylation profile on both normal and tumor bladder tissue samples and on [white blood cells](#) from healthy donors. They identified 1,429 regions that were consistently methylated in all three samples.

They then tested the methylation profile of these 1,429 regions in T24 bladder cancer and HL60 leukemia cell lines treated with a DNMTi for 24 hours. Of these, 79 significantly responded to demethylation treatment and remained demethylated beyond 30 days. Further analysis focused on the top two regions, which showed consistent hypermethylation in normal and tumor samples.

To verify their findings, Yang and colleagues studied the DNA demethylation levels of those two markers in urine samples from seven patients with MDS treated with the DNMTi azacitidine. They found that the two markers were significantly demethylated, in contrast to LINE-1 methylation, which showed no clear decreasing trend.

According to Yang, these findings could lead to the use of a simple urine test for detecting response to a DNMTi.

Provided by American Association for Cancer Research

Citation: More accurate markers identified for detecting response to epigenetic drugs for myelodysplastic syndromes (2013, April 8) retrieved 6 May 2024 from

<https://medicalxpress.com/news/2013-04-accurate-markers-response-epigenetic-drugs.html>

This document is subject to copyright. Apart from any fair dealing for the purpose of private study or research, no part may be reproduced without the written permission. The content is provided for information purposes only.