Right warfarin dose determined by 3 genes

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Researchers at Uppsala University, together with colleagues at the Karolinska Institute and the Sanger Institute, have now found all the genes the determine the dosage of the blood-thinning drug warfarin. The findings are published in the scientific journal *PLoS Genetics*.

"We have previously studied selected genes that can affect warfarin treatment. Now that we have gone in and scanned the entire genome, we see that the two most important genes are among those we previously singled out," says Mia Wadelius, a researcher at Uppsala University, and one of the scientists behind the study.

She also says that this is the first truly large warfarin study in which all genes were reviewed at the same time. More than 1,000 warfarin patients and roughly 370,000 gene variants, covering the entire human genome, were studied.

"The adequate warfarin dosage for a patient is determined by three genes: VKORC1, CYP2C9, and CYP4F2. This is a step forward for a large group of patients, because it will be easier to determine the dosage, and the treatment will be less risky," says Mia Wadelius.

Patients vary in their sensitivity to warfarin, which makes treatment initially a risky balancing act between bleeding and blood clots. Mia Wadelius says that the variation is great among patients, sometimes up to a difference of twenty times. But now that researchers have managed to identify which genes underlie this variation, it will be possible to predict different patients' needs for warfarin more precisely, rendering

treatment safer. The next step is to look for markers for bleeding.

"We will continue to look for genetic variants that influence the risk of bleeding, which can be a reaction to warfarin treatment, though a rare one. The findings of the Swedish study will be combined with those from a British study in order to attain a sufficiently robust analysis of risks of bleeding," says Mia Wadelius.

Source: Uppsala University