Synthesis of Analogues of S-adenosyl-L-methionine for Identification of WBSCR27 Substrate

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WBSCR27-methyltransferase is associated with Williams syndrome. Williams syndrome is a genetic disease that is accompanied by a number of severe symptoms, including mental retardation, cardiovascular diseases, hypercalcemia, and many others that lead to a decrease in the life expectancy of patients. It is important to know the specific functions of proteins that are absent in patients with Williams syndrome. In the case of WBSCR27, we have to understand the nature of the methylation substrate. The approach of this work is to modify the coenzyme S-adenosyl-L-methionine (SAM), which is a donor of the methyl group. In this work, an analog of S-adenosyl-L-methionine (SAM) was synthesized, which contains a vinyl fragment instead of the methyl group (CH3) (S-adenosyl-L-vinthionine (SAV)). Such a fragment could be alkylated by the substrate because of its nucleophilic properties. That could be another way to selectively isolate substrate from the cell lysate. The binding of WBSCR27 and SAV was shown by NMR spectroscopy of a mixture of SAV and 15N-WBSCR27 obtained earlier. We have also made the first experiments using SAV and eukaryotic cells lysate. The differences between the results of the preliminary experiments and the control line indicate that a possible substrate for methylation by WBSCR27 enzyme is RNA.

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