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ACCEPTED MANUSCRIPT

Title: An optimized method using peptide arrays for the identification of *in vitro* substrates of lysine methyltransferase enzymes

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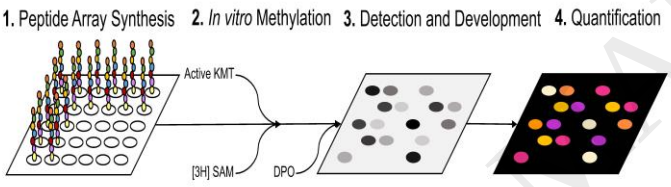
Graphical abstract



Abstract
While a number of post-translational modifications (PTM), such as phosphorylation and ubiquitination, have been extensively studied, lysine methylation is emerging as an important PTM with implications in a growing number of diverse cellular processes. To date, there are approximately 5,000 identified methylation sites on non-histone proteins, and as the methyllysine proteome expands it becomes important to identify the lysine methyltransferase enzymes responsible for each methylation event. The use of peptide SPOT methylation assay has proven to be a useful in the identification and validation of novel substrates for lysine methyltransferase enzymes as it uses a weak beta emitter coupled with fluorography to detect methylation events. The method described in this paper provides improvements to the typical protocol for this assay, as a highly sensitive tritium assay can be developed with less radioactivity than previously described. This

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