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## **Comprehensive response of HIV-infected human primary macrophages to methamphetamine exposure**

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**Background and significance:** Use of Methamphetamine (Meth) causes multiple global health problems including negative effects on the immune system. Because of such impairments, Meth users suffer from comorbid infections.

**Hypothesis:** Exposure of human monocyte-derived macrophages (hMDM) to Meth leads to impairment of their functions as a part of the innate immunity system.

**Results:** Comparison of proteome profiles of CIC, CIM and MIM. CIC denotes condition in which infection only occurs; CIM denotes Meth treatment post-infection. MIM represents Meth treatment before and after infection. hMDM from 7 donors were used to perform targeted and untargeted LC-MS/MS analyses revealed proteins, which levels vary across the investigated conditions. Among them we verified a set of 11 Ras-related Rab proteins using LC-MRM-MS approach and proved that indeed they levels differ between CIC, CIM and MIM, but the patterns of these differences also vary across the donors. Based on the differences in post-translational modifications between CIC, CIM and MIM hMDM, we choose acetylated lysine K15 of histone H3 for further validation and absolute quantification, that has been performed using stable isotope labelled standards and LC-MRM-MS approach.

**Discussion:** Observed effects of Meth on hMDM are multifaceted and we see changes on various levels. We are making a substantial progress in combining comprehensive investigations of how Meth affects hMDM which are central for the innate immunity system. Our results provide new information about cell biology of hMDM under an insult of Meth as well as provide refined methodologies for analytical measurements and validation across samples and platforms.