Retrovirology

Poster presentation

N-myristoyltransferase1 and N-myristoyltransferase2 Exhibit Differential Substrate Specificity for HIV-Gag and HIV-Nef

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Background

N-terminal myristoylation of Gag and Nef plays a critical role in retroviral virulence and budding of newly formed particles. Myristoylation involves the transfer of a myristate moiety from myristoyl-CoenzymeA (myristoyl-CoA) to substrate proteins such as Gag and Nef. Two isozymes accomplish this process in humans, and are known as N-myristoyltransferase1 (NMT1) and N-myristoyltransferase2 (NMT2). We used a biochemical approach to determine myristoylation kinetics for Gag and Nef as well as preferential substrate specificity for NMT1 or NMT2.

Materials and methods

NBD-labeled peptides containing the myristoylation sequence for Gag or Nef were myristoylated by recombinant NMT1 or NMT2 and subsequently analyzed by HPLC analysis.

Results

Results of the kinetics studies (K_m, K_{cat}, catalytic efficiency, turnover number, etc.) indicate that both isozymes prefer Nef up to 150 times vs. Gag as a substrate. Both isozymes also exhibit greater catalytic efficiency in myristoylating Nef. Interestingly, Nef is preferentially myristoylated when Gag is present in the system.

Conclusion

This study is the first report of a differential role of NMT1 and NMT2 in the myristoylation of retroviral proteins and provides a new target in the treatment of HIV.