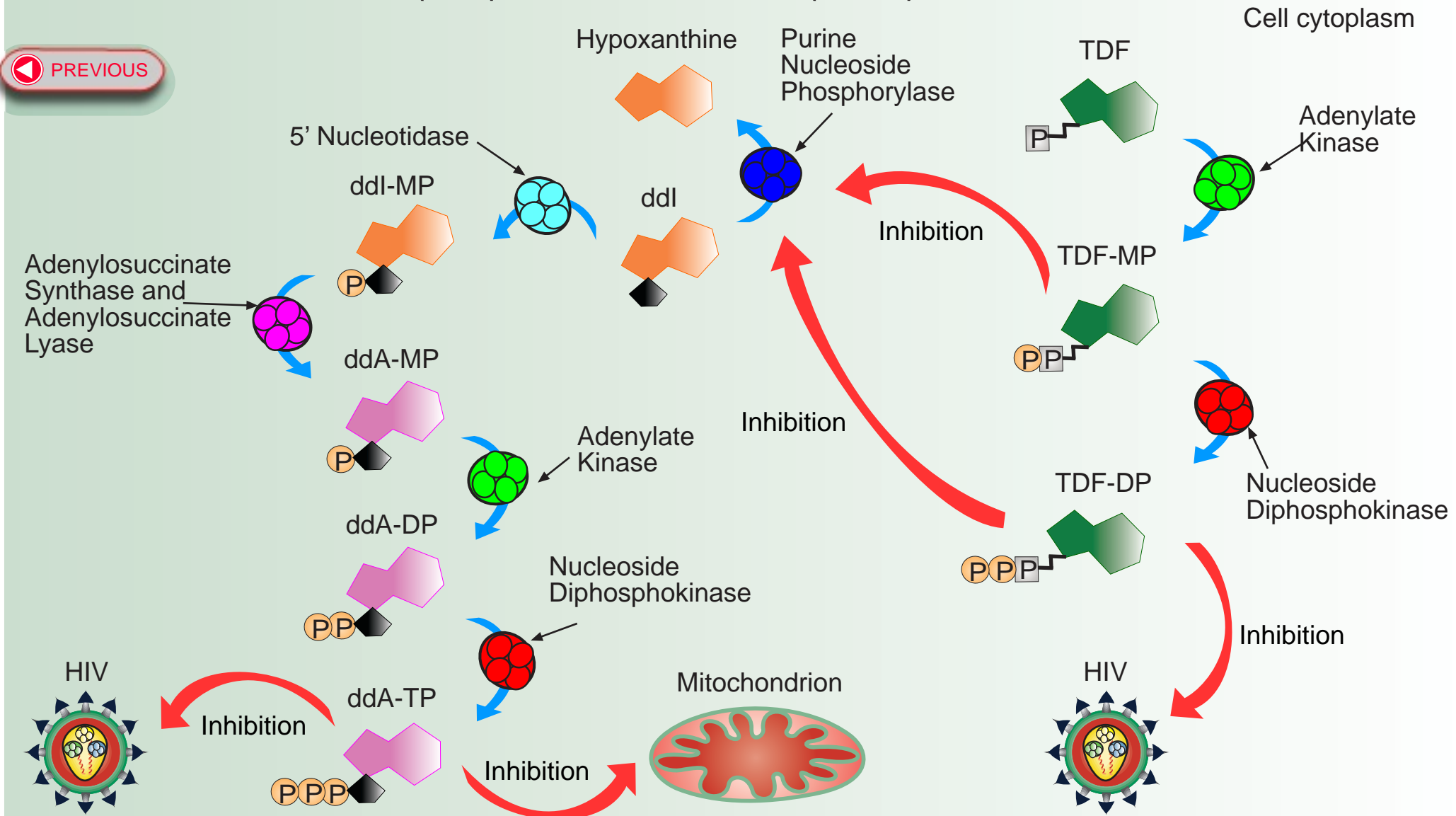


Didanosine (ddI) and Tenofovir (TDF) metabolism



Cellular enzymes metabolise tenofovir (TDF) and generate mono- and diphosphates which are both inhibitors of purine nucleoside phosphorylase (PNP). PNP normally metabolises cellular inosine monophosphate (IMP). ddI is a substrate competitor against IMP since ddI is also a substrate of PNP. Inhibition of PNP leads to higher intracellular levels of ddI which is converted to dideoxy-ATP (ddATP) by cellular enzymes. HIV replication is inhibited by ddATP and tenofovir diphosphate, however mitochondrial polymerase gamma is also inhibited by ddATP and results in higher levels of mitochondrial toxicity.

