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Some HIV protease inhibitors have also other beneficial, non-virological effects with potential therapeutic applications

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The introduction of HIV-protease inhibitors (PIs) in antiretroviral therapy drastically diminished the incidence, prevalence and severity of opportunistic infections. These beneficial effects are primarily due to immune reconstitution following the decrease of HIV replication. We reported that some PIs increase the RALDH's activity and consequently augment the production of retinoic acid (RA) *in vitro*. We demonstrated that *in vivo*, PIs (as part of an optimal antiretroviral therapeutic regimen) decrease serum RA concentrations. These discrepancies of *in vivo* and *in vitro* data are due to the fact that RA synthesis and its alteration by PIs take place intracellularly. Elevated intracellular RA level increases its own catabolism and inhibits (feedback) its synthesis. Based on these and other published data we have suggested that altered RA metabolism by PIs might affect the expression of retinoid-responsive genes and retinoid-mediated signaling pathways. Several beneficial effects of PIs, such as improvements in the control of certain infections of HIV-associated nephropathy (HIVAN), Kaposi's sarcoma, other cancers, HIV-dementia, HIV-associated colitis, etc., could be partially explained by their direct effect on RA synthesis. Moreover, therapeutic uses of synthetic retinoids have been proven efficacious in the treatment of Kaposi's sarcoma and HIVAN and experimentally, RA is synergistic with primaquine against *Pneumocystis*. PIs also inhibit the aspartyl proteases of several parasites and fungi as documented by numerous publications. And finally, other effects such as inhibition of the proteasome-ubiquitin process and diminished apoptosis are now exploited for the treatment of different cancers and neurodegenerative disorders.

Biography

Maude Loignon has completed her MSc in 2007 and her MD in 2012. She is now a 3rd year Resident in Microbiology and Infectious Diseases at the University of Montreal, Canada. She has published 7 papers in peer-reviewed journals.

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