

## **ANTIRETROVIRAL TREATMENT CAN AFFECT THE RELEASE OF NO AND EDCF, BUT NOT EDH IN RAT ARTERIES**

*Arslan Nejad, Shui S Lee, Paul M Vanhoutte, Susan WS Leung*

1 Pharmacology & Pharmacy, University of Hong Kong, China; 2 Faculty of Pharmaceutical Sciences, University of Copenhagen, Denmark; and 3 Department of Microbiology, Chinese University of Hong Kong, China

Despite improving clinical outcomes, highly active antiretroviral therapy (HAART) is an independent potential risk factor for cardiovascular diseases. Currently the recommended HAART regimen commonly comprises a protease inhibitor (PI) with ritonavir (RTV)-boosting or a non-nucleoside reverse transcriptase inhibitor (NNRTI), and two nucleoside reverse transcriptase inhibitors. The present study examined whether or not boosted lopinavir (LPVr), a PI, and/or efavirenz (EFV), an NNRTI, affect the regulation of vascular tone in ways leading to cardiovascular complications. Male Sprague Dawley rats were treated with LPVr (80/20 mg/kg), RTV (20 mg/kg), EFV (160 mg/kg) or the vehicle methylcellulose (0.5%) once daily by oral gavage two weeks after they were fed normal or high fat diet. After eight weeks of antiretroviral treatments, superior mesenteric arteries were isolated and suspended in organ chamber for the study of vascular reactivity. Endothelium-dependent relaxations to acetylcholine were not different between rats fed with normal and high fat diet. None of the antiretroviral treatments affected acetylcholine-induced relaxation in rats fed with normal diet. However, RTV significantly reduced acetylcholine-induced relaxation in rats fed with high fat diet. This reduction was not observed in arteries incubated with indomethacin. By contrast, LPVr enhanced acetylcholine-induced nitric oxide (NO)-mediated relaxation in the high fat group. Endothelium-dependent hyperpolarization-mediated relaxations were not affected by these antiretroviral treatments. As a result, chronic treatment with RTV may cause cyclooxygenase-dependent contractions in rats with high fat. While RTV impairs vascular relaxation, its combination with lopinavir does not cause vascular dysfunction, probably because lopinavir causes activation of NO signalling pathway.