Background: Nitrate tolerance is associated with an enhanced superoxide anion produc-
tion and could be attenuated by statins as they interact with the two main (eNOS and
NAD(P)H oxidase) pathways involved in this oxidative stress.
Methods: 3 groups of normocholesterolemic rats were treated: group 1 received rosuvas-
statin (10 mg/kg/d post for 5 weeks) and the last 3 days a cotreatment with the statin plus
nitroglycerin (NTG 50 mg/kg/d, sub-cutaneous injection b.i.d); group 2 received only
NTG (50 mg/kg/d, b.i.d. for 3 days) and group 3 served as control. Rings of thoracic aor-
tas from these rats were used.购房者
Results: In group 2 (NTG), the concentration-response curves to NTG were significantly
shifted to the right (IC50 NTG concentration needed to evoke a half-maximal relaxation)
was 6.76±0.06 (n=7) > 7.77±0.08 (n=3) in group 3 (not exposed to NTG, P<0.01); 
O2- production was enhanced (289±23 (n=6) vs 183±34 (n=5, P<0.05). In contrast, in
group 1, the rightward shift was attenuated (IC50 values was 7.19±0.11 (n=8), P<0.05 vs
group 2); O2- production was decreased : 208±19 (n=6, P<0.05 vs group 2). In addition,
before NTG exposure, rosuvastatin treatment decreased p22phox (the essential
NAD(P)H oxidase) subunit abundance in aortic wall and NAD(P)H oxidase activity. In contrast,
this treatment did not alter either eNOS abundance or the basal release of endothelium-
derived NO.
Conclusion: Long-term rosuvastatin treatment protects against nitrate tolerance by coun-
tering NTG-induced increase in O2- production. This protection seems to involve a
direct interaction with the NAD(P)H oxidase pathway rather than an upregulation of
the eNOS pathway.

Enhancing Arteriogenesis Increases Atherosclerosis and Reducing Atherosclerosis Reduces Arteriogenesis: Demonstration of the Concept in Mice
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Background: Inflammatory and immune cells are known to contribute to atherogenesis.
We have reported data indicating that such cells also enhance collateral development.
We have used two mouse models with different predispositions to both ath-
erosclerosis and collateral development to gain insight into this “trade-off” phenomenon.
It is our hypothesis that: Shared inflammatory mechanisms contribute to both atheroscler-
sis and to arteriogenesis; stimulating these pathways will activate both processes.
Consideration of these findings will be important in developing clinical strategies designed
to enhance collaterals or prevent atherosclerosis in patients.
Methods: Aortic lesion area was assessed in 16 week, chow fed Balb/c and C57BL/6J
Apoe- mice. In order to assess whether IC50 for DMSO staining and TF staining were
affected. Consideration of these findings will be important in developing clinical strategies
to enhance collaterals or prevent atherosclerosis in patients.
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