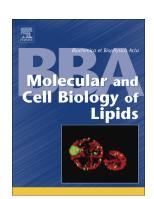
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ACCEPTED MANUSCRIPT

Regulatory effects of simvastatin and apoJ on APP processing and amyloid-β clearance in blood-brain barrier endothelial cells

Martina Zandl-Lang¹, Elham Fanaee-Danesh¹, Yidan Sun¹, Igor Čančar¹, Chaitanya Chakravarthi Gali¹, Alexandra Kober¹, Nicole M Albrecher¹, Carmen Tam-Amersdorfer¹, Anika Stracke¹, Steffen Storck², Ahmed Saeed³, Jasminka Stefulj⁴, Claus Pietrzik², Mark R Wilson⁵, Ingemar Björkhem³, Ute Panzenboeck^{1*}

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Highlights:

- Simvastatin shifts APP processing towards the non-amyloidogenic pathway in pBCEC
- Inhibition of cholesterol synthesis by simvastatin up-regulates apoJ in pBCEC
- Both, simvastatin and apoJ increase expression of APP and reduce Aβ uptake in pBCEC
- Increased Aβ and simvastatin induce LRP1 and apoJ levels in vitro and in vivo
- Thereby clearance of Aβ across the blood-brain barrier is facilitated

Keywords: Alzheimer disease, amyloid-beta (A β), endothelium, cholesterol metabolism, blood-brain barrier, clusterin/apoJ

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