# Effect of Pravastatin on placental expression of EGFL7 in preeclampsia and intrauterine growth restriction: a new potential therapeutic approach

Stefano **Fruci** [1,*], Micol **Massimiani** [2,3], Silvia **Salvi** [1], Heidi **Stuhlmann** [4], Hebert **Valensise** [5,6], Antonio **Lanzone** [1,7], Sergio **Ferrazzani** [1,7], Luisa **Campagnolo** [3]

[1] UOC of Obstetric Pathology, Department of Women's Health, Child Health and Public Health, Fondazione Policlinico Agostino Gemelli, IRCSS, Rome, Italy.
[2] Saint Camillus International, University of Health Sciences, Rome, Italy,
[3] Department of Biomedicine and Prevention, University of Rome Tor Vergata, Rome, Italy.
[4] Department of Cell and Developmental Biology, Weill Cornell Medical College, New York, U.S.A.
[5] Department of Obstetrics and Gynaecology, Policlinico Casilino, Rome, Italy.
[6] Obstetrics and Gynaecology Unit, Department of Surgical Sciences, University of Rome Tor Vergata, Rome, Italy.
[7] Università Cattolica del Sacro Cuore, Rome, Italy.

**DOI:** 10.36129/jog.2022.S14

**Objective**. Epidermal Growth Factor Like Domain 7 (EGFL7) is an angiogenic factor that we have recently identified in human placenta trophoblast. In pregnancies complicated by preeclampsia (PE) a significant EGFL7 downregulation in placental tissues is on the other hand accompanied by a significant increase in maternal plasma. Circulating EGFL7 can differentiate early- and late-onset PE (e-PE and l-PE) and isolated intrauterine growth restriction (IUGR) from e-PE. Pravastatin (PRA) is a lipid-lowering drug whose potential in the prevention and treatment of PE has been highlighted. The aim of our study is to evaluate the ability of PRA to modulate EGFL7 expression in human chorionic villous explant cultures from uncomplicated and PE- and IUGR affected pregnancies.

**Materials and Methods**. 19 women were enrolled for this study: 10 healthy controls, 4 e-PE, 3 l-PE and 2 IUGR. Chorionic villous explants were cultured for 24 hours with or without 10 μM PRA. The gene and protein expression of EGFL7 and other angiogenic factors were quantified by qRT-PCR and Western Blot analysis.

**Results**. PRA significantly increased EGFL7 gene expression in cultures obtained from healthy, l-PE and IUGR pregnancies ($p < 0.001$, $p = 0.006$, and $p = 0.014$, respectively), while its levels decreased in e-PE villi after PRA treatment ($p = 0.025$). This trend was confirmed at protein level.

**Conclusions**. Pravastatin is able to modulate the expression of EGFL7 in human placenta; the differences observed between l-PE and e-PE underlines once again the well-known different nature of the two forms of PE and isolated IUGR.