Chasing novel biomarkers to predict preterm and term preeclampsia
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Objective
To determine serum levels of growth differentiation factor 15 (GDF15) in the third trimester in women presenting with preeclampsia and investigate whether changes in GDF15 depend on preeclampsia (PE) subtype (early-onset vs late-onset). Also, to establish whether two HtrA3 ELISAs tests would provide useful tools for early detection of PE during the first trimester.

Methods
Serum samples across three trimesters from 29 healthy pregnancies, third trimester sera from 34 women presenting with preeclampsia (early-onset n = 16, late-onset n = 18) and 66 gestation-age matched controls were examined for GDF15 by ELISA. Furthermore, using highly specific HtrA3 monoclonal antibodies, we established and fully validated two enzyme-linked immunosorbent assays to detect both HtrA3 isoforms together (HtrA3-T) and HtrA3-L alone in the human serum. We then determined serum HtrA3 at 11 to 13 weeks of gestation in a cohort of singleton pregnancies that proceeded without complications or developed preeclampsia in the third trimester.

Results
Serum GDF15 levels increased significantly with gestation in normal pregnancy. GDF15 was significantly reduced in the third trimester in women presenting with preeclampsia compared to their gestation-age-matched controls. This reduction was apparent in both early-onset and late-onset subtypes, but it was more profound in late-onset cases. Furthermore, compared with controls, those who developed late-onset preeclampsia had significantly higher levels of HtrA3-L, whereas those who developed early-onset preeclampsia had significantly lower ratios of HtrA3-L/HtrA3-T.

Conclusion
GDF15 was significantly reduced in the third trimester in women presenting with preeclampsia, especially in late-onset cases. HtrA3 has potential utility for first trimester prediction of preeclampsia. These two potential novel markers should be tested in conjunction with previously described multifactorial predictive models (FMF algorithms) to assess their performance to predict preterm and term preeclampsia in future studies.