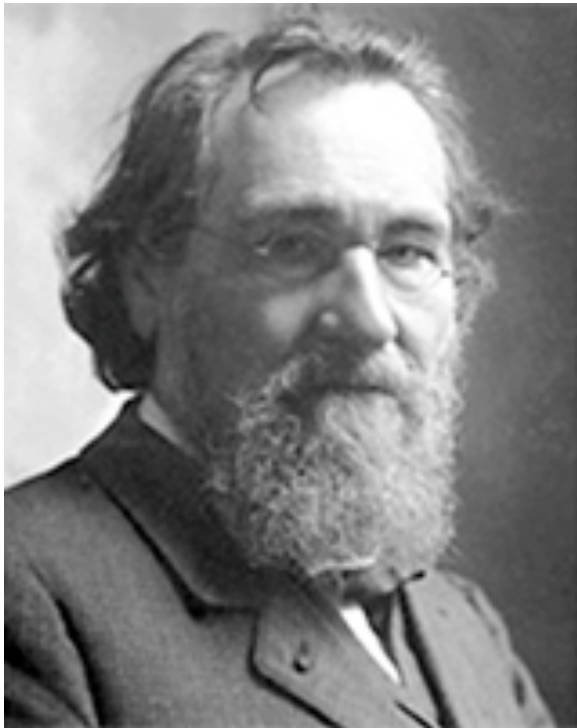


Long-held dogma that the womb is sterile and invasion of bacteria from vaginal tract can drive APOs.



Mechanisms of Disease

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INTRAUTERINE INFECTION AND PRETERM DELIVERY

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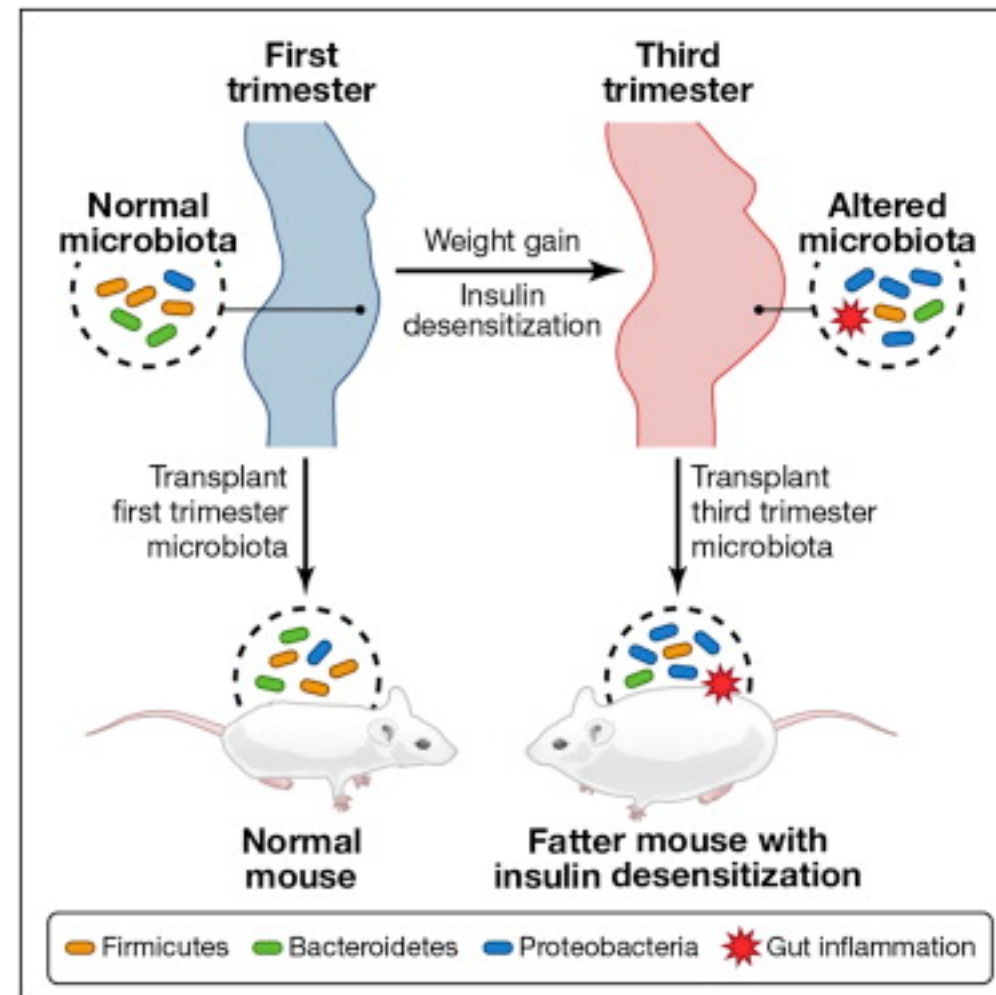
French pediatrician Henry Tissier declared unborn babies bacteria-free [1].

Bacterial invasion of sterile womb, likely from vaginal track, is a driver of adverse pregnancy outcomes (APOs). [2].

[1] http://www.nytimes.com/2013/08/29/science/human-microbiome-may-be-seeded-before-birth.html?_r=0

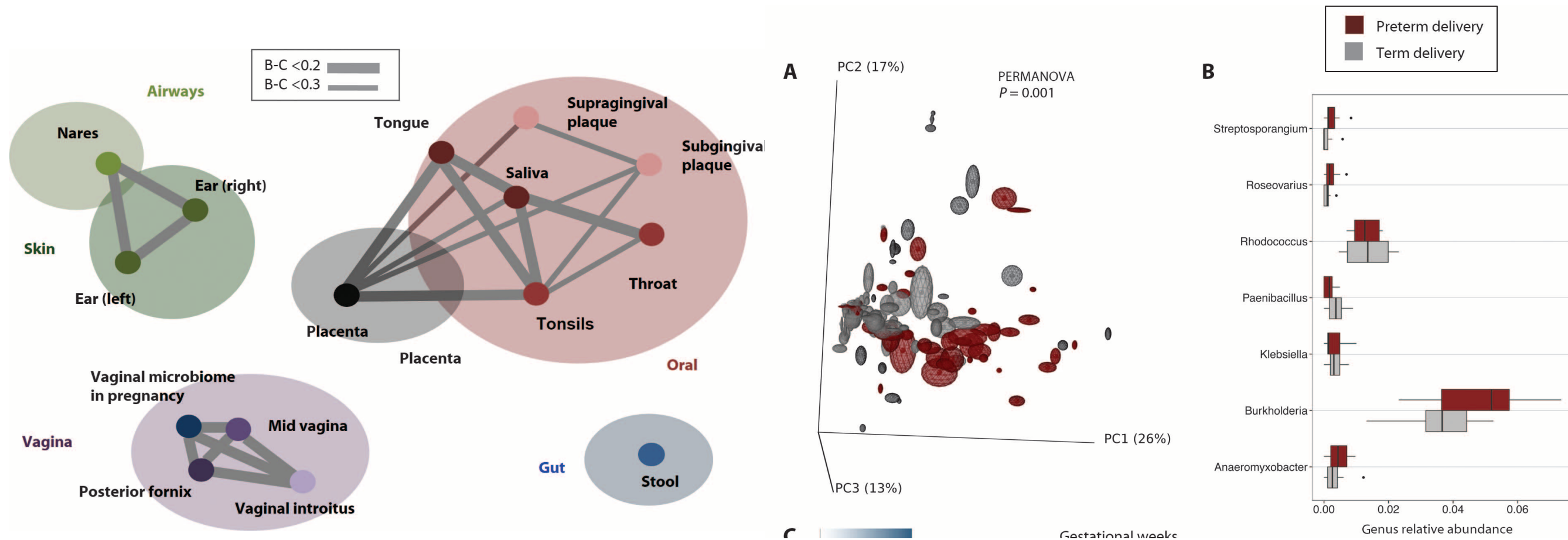
[2] <http://www.nejm.org/doi/full/10.1056/NEJM200005183422007>

High-throughput sequencing has shown that human uBiome changes over the course of pregnancy.



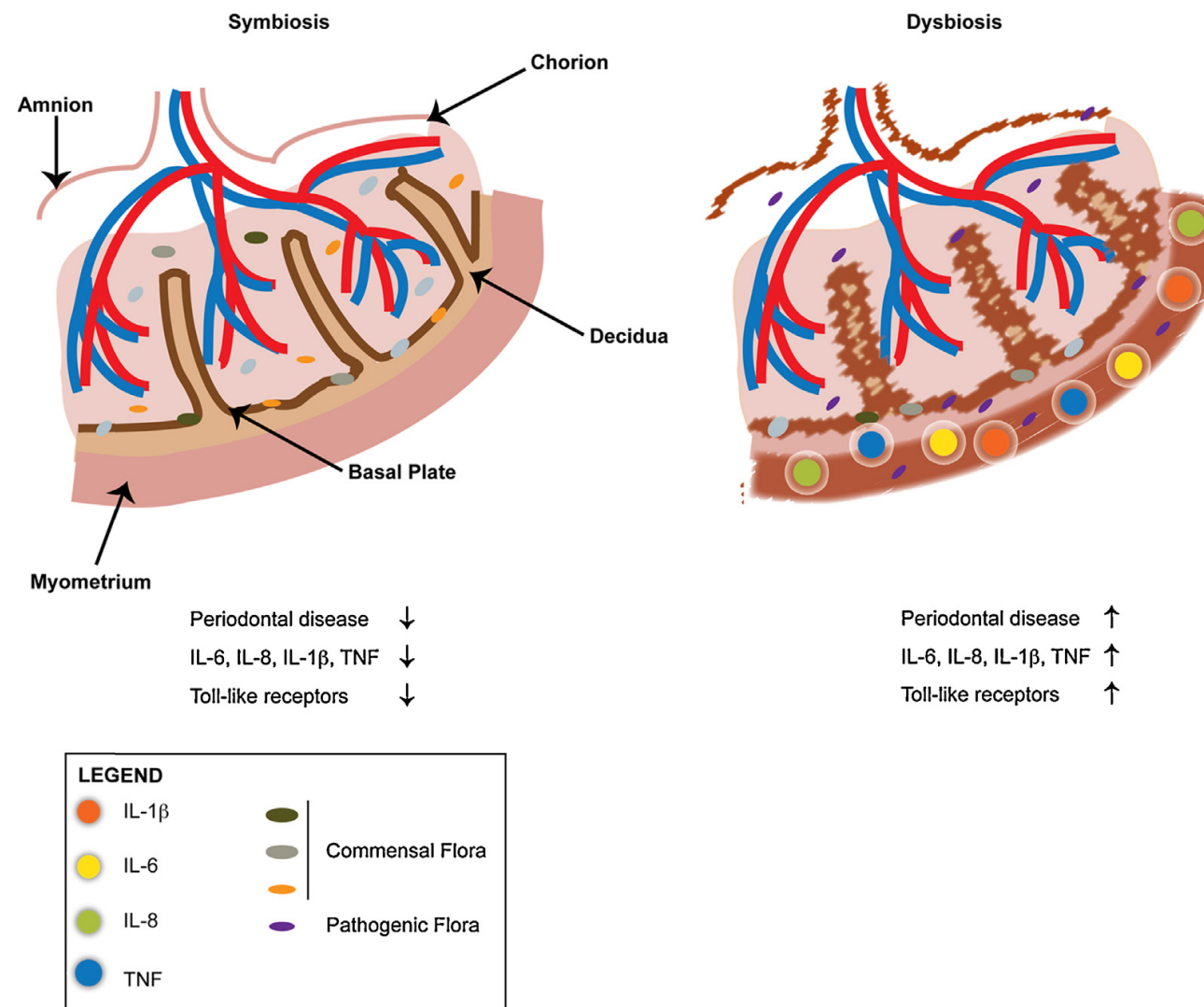
Significantly altered human gut microbiome over the course of pregnancy in cohort of 91 subjects. T3 uBiome reduces insulin sensitivity and promotes adiposity. Excess adiposity and loss of insulin sensitivity are beneficial in the context of a normal pregnancy, as they support fetus growth and prepare body lactation.

High-throughput sequencing also shows womb is not sterile, can seed fetus, and may affect APOs.



Deep sequencing of placental microbiome in cohort of 320 subjects shows similarity to Oral cavity and suggests that perturbation of placental microbiome could lead to APOs.

Alteration in placenta community structure, potentially via bugs from distal body sites, could drive APOs.



A model of broad interest is that dysbiosis of placental microbiome, driven by migration of pathogens (or other factors), can affect pregnancy outcomes [3]. Mouse studies support this, as migration of oral pathogens via blood to placenta can drive APOs [1,2].

[1] <http://www.ncbi.nlm.nih.gov/pubmed/15039352>

[2] <http://www.ncbi.nlm.nih.gov/pubmed/22040113>

[3] <http://www.sciencedirect.com/science/article/pii/S0165037814000357>

Opportunities

Context: Cohort of 48 subjects with high-throughput microbial sequencing of vagina, oral, and gut (~200 samples) collected over the course of pregnancy along with matched sequencing of blood samples (~60 samples).

- (1) Unsupervised learning: How does the structure of each body site change with respect to pregnancy. Based upon prior work, we expect to see changes in gut and vagina, minimally. Any observations about changes in blood will be novel.
- (2) Supervised learning: Does the microbiome composition at body sites predict that of blood? The relationship between body sites and blood is of high interest given the possibility of microbial migration through blood between body sites and placenta.