Study identifies possible causes of and protectors against premature birth

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Seven types of bacteria and certain immune factors in a woman's vagina and cervix may be responsible for increasing the risk of spontaneous preterm birth (sPTB) or protect against it, according to a new study from the Perelman School of Medicine at the University of Pennsylvania and the University of Maryland School of Medicine. Results of the study

provide groundbreaking information that the authors suggest could help physicians better predict preterm birth, especially for African-American women early in pregnancy. The study, published today in *Nature Communications*, will allow for the development of new research targeting "bad" bacteria or increasing "protective" bacteria.

"The results of this study give us a break we've been working toward for many years. Previous research suggested that the cervical vaginal microbiome is different in women who experience preterm birth but those studies had small numbers of women and were not conclusive. With this large cohort, for the first time, we're actually able to show the 'specific microbial signatures' that are involved in preterm birth," said lead author Michal Elovitz, MD, a professor of obstetrics and gynecology at Penn Medicine and principal investigator of this study. Elovitz is also a co-investigator for the March of Dimes' Prematurity Research Center at the University of Pennsylvania which helps to support other mechanistic studies on the vaginal microbiome and preterm birth.

Spontaneous preterm birth (sPTB), defined as birth before 37 weeks of gestation, and its complications, are the largest contributors to infant death in the United States and worldwide. Babies who survive an early birth often face serious, costly and lifelong health problems, including breathing problems, vision loss, cerebral palsy and intellectual delays. The economic burden of preterm birth is staggering, with an estimated cost of $26 billion per year in the United States alone. A failure to predict and understand the causes of preterm birth has limited the development of effective interventions and therapies.

In the new study, researchers examined vaginal swabs from a sample of 2,000 pregnant women, taken at three distinct points in pregnancy, to identify the bacteria that make up the cervicovaginal microbiota. The data comprise the largest sample of cervicovaginal microbiota in

pregnant women to date. Using an innovative Bayesian modeling of the cervicovaginal microbiota, seven bacteria were found to significantly increase the risk of sPTB, with a stronger effect seen in African American women. Higher vaginal levels of the antimicrobial peptide β-defensin-2, a part of our innate immune system, lowered the risk of sPTB associated with cervicovaginal microbiota. The protective effect of this immune marker was greater in African American women.

The findings hold promise for the development of diagnostics to accurately identify women at risk for sPTB early in pregnancy. Importantly, this study provides new insights into causes for the significant racial disparity observed in preterm births. Therapeutic strategies could include immune modulators and microbiome-based therapeutics to reduce this significant health effect.

More information: Michal A. Elovitz et al, Cervicovaginal microbiota and local immune response modulate the risk of spontaneous preterm delivery, *Nature Communications* (2019). DOI: 10.1038/s41467-019-09285-9 , dx.doi.org/10.1038/s41467-019-09285-9

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