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Directional selection of Large White pigs for gut microbiota enterotypes

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Studying the influence of host genetics on gut microbiota composition is challenging because it is difficult to dissociate the variability due to genetic effects from the variability due to the environment, notably the maternal microbial environment at birth. Thus, we launched a study to demonstrate coevolution of the host and its gut microbiota by directional selection over two generations. We have shown the existence of two enterotypes on populations of 60-day-old piglets (d60) by sequencing the 16S rRNA gene from fecal DNA. These enterotypes are characterized by differential abundances of the genera *Prevotella* and *Mitsuokella* (PM enterotype) or *Ruminococcus* and *Treponema* (RT enterotype). We have started a selection experiment by generating two pig lines contrasting for their enterotype. In the initial population (generation G0), we studied 317 piglets and confirmed a stratification according to the PM or RT enterotype at d60. The founders for the next generation (G1) were selected among the G0 population for their higher abundance in *Prevotella* and *Treponema* for the lines PM and RT, respectively (6 males and 30 females per line). Each male inseminated five females from the same line, and four piglets were sampled at d60 for fecal microbiota composition analysis. We showed significant differences between the two lines in the relative abundance of the four bacterial genera that characterize the enterotypes ($P < 0.001$, from 0.6 genetic standard deviation for *Treponema* to 1.3 for *Prevotella*). The observed contrasts were in the expected direction, thus demonstrating a response to selection consistent with the expected genetic response. The heritabilities of the relative abundance of the bacterial genera were estimated by combining G0 and G1 animals (588 piglets): $h^2 = 0.30$ for *Prevotella*, $h^2 = 0.31$ for *Ruminococcus*, $h^2 = 0.39$ for *Treponema*, $h^2 = 0.35$ for *Mitsuokella*. All these results demonstrated a significant influence of host genetics on the composition of gut microbiota at d60 in pigs and a capacity of directional selection over generations.