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## **The molecular basis of the degradation of flavan-3-ols by the human gut bacterium *Eggerthella lenta***

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Flavan-3-ols are among the most consumed polyphenols by humans and have been shown to prevent cardiovascular diseases. They are found in plant as monomers and mainly as oligomers such as procyanidins. The majority reaches the colon where the microbiota converts them into phenolic metabolites likely to participate in their health effects. While the metabolic pathways of the degradation of flavan-3-ols by the microbiota are relatively well described, only a few microorganisms and microbial genes involved in these pathways are known. We have previously shown that *Eggerthella lenta* metabolizes flavan-3-ol monomers and oligomers. Here, our aim was to identify *E. lenta* genes encoding enzymes degrading flavan-3-ols and to determine their prevalence in human gut metagenomes.

By a transcriptomic approach (RNAseq) carried out with the type strain of *E. lenta*, coupled with the heterologous expression of the genes of interest in *Escherichia coli*, we have discovered two genes (*fmber1*, *fmber2*) encoding two benzyl ether reductases cleaving the C ring of the monomers and an operon of two genes (*pber*) catalyzing this reaction on the dimers of type-B procyanidins. Furthermore, two operons of three genes (*cadh*, *ecadh*) encoding enzyme complexes dehydroxylating the B-ring of (+)-catechin and (-)-epicatechin have also been identified. These genes constitute good markers of flavan-3-ol metabolization in the gut. Their prevalence in human gut metagenomes suggested that 27% of individuals cannot convert flavan-3-ols into potential bioactive metabolites. These results raise the question of whether individuals who do not harbor these bacterial genes are at greater risk of developing cardiovascular disease.