Molecular characterization of a new gene cluster for steroid degradation in Mycobacterium smegmatis

The C-19 steroids 4-androstene-3,17-dione (AD), 1,4-androstadiene-3,17-dione (ADD) or 9-hydroxy-4-androstene-3,17-dione (9OH-AD), which have been postulated as intermediates of the cholesterol catabolic pathway in Mycobacterium smegmatis, cannot be used as sole carbon and energy sources by this bacterium. Only the kstR mutant which constitutively expresses the genes repressed by the KstR regulator can metabolize AD and ADD with severe difficulties but still cannot metabolize 9OH-AD, suggesting that these compounds are not true intermediates but side products of the cholesterol pathway. However, we have found that some M. smegmatis spontaneous mutants mapped in the PadR-like regulator (MSMEG_2868) can efficiently metabolize all C-19 steroids. We have demonstrated that the PadR mutants allow the expression of a gene cluster named C-19+ (MSMEG_2851 to MSMEG_2901) encoding steroid degrading enzymes, that are not expressed under standard culture conditions. The C-19+ cluster has apparently evolved independently from the upper cholesterol kstR-regulon, but both clusters converge on the lower cholesterol kstR2-regulon responsible for the metabolism of C and D steroid rings. Homologous C-19+ clusters have been found only in other actinobacteria that metabolize steroids, but remarkably it is absent in Mycobacterium tuberculosis.

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