

CLONING AND CHARACTERIZATION OF *argC* GENE OF *Streptomyces clavuligerus*.

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S. clavuligerus is a producer of the β -lactam antibiotic cephamycin C and the β -lactamase inhibitor clavulanic acid. Arginine and/or ornithine are precursors of the clavulanic acid molecule and stimulate the production of clavulanic acid (Romero et al, Appl. Env. Microbiol. 52, 892, 1986). We are interested in elucidating the relationship between the arginine biosynthetic pathway and antibiotic production in *S. clavuligerus*.

A previously uncharacterized arginine auxotrophic strain, *Streptomyces lividans* 1674, was found to be complemented by an 1.8 Kb DNA fragment containing the *argC* gene of *E. coli* (Crabeel et al, Gene 5, 207, 1979). Shotgun cloning of partially *Sau3A* digested total DNA of *S. clavuligerus* in plasmid pIJ699 and transformation of *S. lividans* 1674 led to a prototrophic transformant containing plasmid pULML30 with a 3.2 Kb DNA insert. The recombinant plasmid complements not only *S. lividans* 1674 but also *E. coli* XC33 *argC*⁻ and hybridizes with the *argC* gene of *S. coelicolor* (S. Baumberg, unpublished) but not with the *argC* gene from *E. coli*. Restriction analysis of the fragment with several endonucleases and sequencing allowed to locate the *argC* gene in the 3.2 Kb fragment.

N-acetylglutamate- γ -dehydrogenase activity is practically undetectable in the wild type of several species of *Streptomyces* and in *E. coli* XC33 transformed with the *argC* gene from *S. clavuligerus*, but a higher activity (0.65 μ Mols/min/mg protein) was found in *S. lividans* 1674 transformed with pULML30, an intermediate number copy plasmid. When transformed into a clavulanic acid non producer, arginine auxotrophic mutant, *S. clavuligerus* 328, the 3.2 Kb fragment restores both arginine prototrophy and the ability to produce clavulanic acid to wild type levels.