

**Table S1.  $\beta$ - Lactamases of *S. clavuligerus*<sup>1</sup>**

| Class  | Accession Number | Amino Acids Number   | Characteristics <sup>2</sup>  |
|--------|------------------|----------------------|---|
| A      | WP_003952487     | 322                  | Gene located in the CFM cluster. Contains all conserved class A motifs  |
| A      | WP_003960860     | 309                  | Contain all conserved class A motifs  |
| A-like | WP_003952519     | 458                  | Named ORF12 and Cpe. Contains a transpeptidase domain. Essential for clavulanic acid biosynthesis. Lacks $\beta$ -lactamase activity. Has a weak cephalosporine esterase activity. Located in the CA cluster. Possible biosynthetic enzyme (see text) |
| B      | WP_003952502     | 339                  | MBL-fold superfamily. Putative L-ascorbate metabolism. Located at the CFM cluster   |
| B      | WP_003952945     | 640                  | MBL-fold superfamily. Hydrolase, sulfatase.   |
| B      | WP_009999286     | 295/260 <sup>3</sup> | MBL-fold metallo hydrolase. Identical proteins but different N-terminal end.  |
| B      | WP_003963044     | 509/327 <sup>3</sup> | MBL fold hydrolase. Identical 327 aa at the C-terminal end. Contains all conserved class B motifs.  |
| B      | WP_009996066     | 237/287 <sup>3</sup> | MBL-fold metallo hydrolase. Identical N-terminal 237 amino acids.   |
| B      | WP_003957750     | 241                  | MBL fold metallo hydrolase. Contains all the conserved Class B motifs   |
| B      | WP_003957858     | 307                  | MBL fold metallo hydrolase.   |
| B      | EDY52266         | 265                  | MBL fold metallo hydrolase. Putative AHL lactonase. Contains all the conserved class B motifs   |
| B      | WP_003958219     | 561                  | Ribonuclease J  |
| C      | WP_003954080     | 276                  | Serine hydrolase. pfam00144.  |
| C      | WP_003955804     | 256                  | Serine hydrolase. pfam00144.  |
| C      | WP_003956069     | 175                  | Serine hydrolase.   |
| C      | WP_003956542     | 462                  | Serine hydrolase. Pfam00144   |
| C      | WP_003960268     | 406/420 <sup>3</sup> | Serine hydrolase. pfam00144. Identical proteins, at difference of the N-terminal end.   |
| C      | WP_009996619     | 411/394 <sup>3</sup> | Serine hydrolase. pfam00144. Identical proteins, at difference of the N-terminal end.   |

(1) Modified from Ogawara (2016). (2) The characteristic motifs are indicated only when all

(2) the  $\beta$ -lactamase motifs are present in the enzyme. (3) Amino acids in different sequences of the same protein

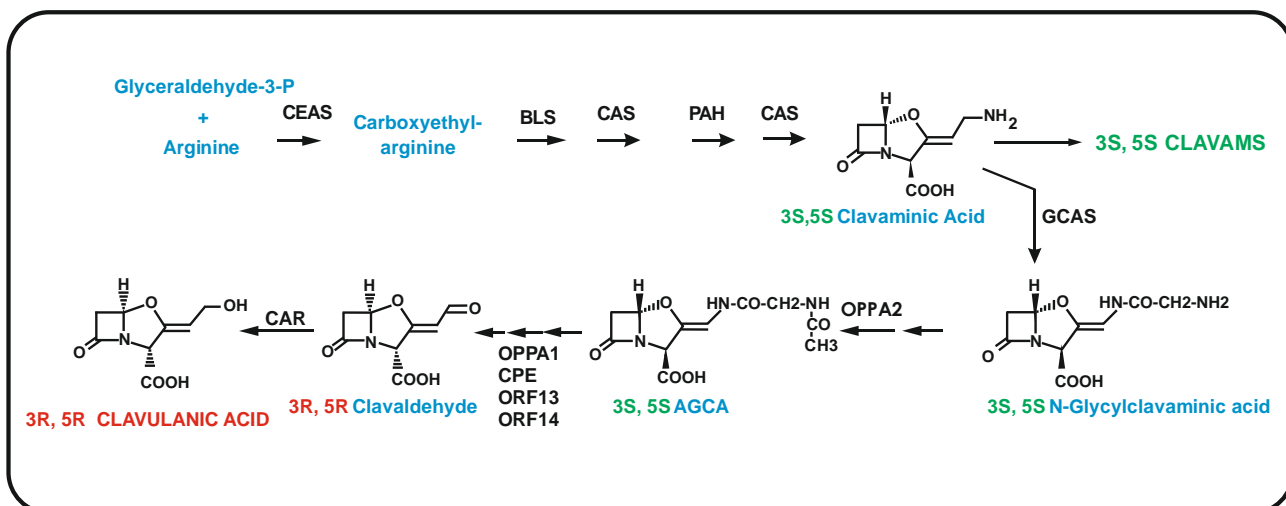


Figure S1. Simplified biosynthetic pathway of clavulanic acid. The intermediate compounds are indicated in blue. The enzymes involved in every step are labelled in black. The final product of the pathway is shown in red letters. Notice that the 3S, 5S configuration in the compounds is labelled in green while the 3R, 5R configuration is labelled in red.