



## Characterization of the Integron Gene Cassettes Harbours Novel Variants of D-Alanine-D-Alanine Ligase Confer High-level Resistance to D-Cycloserine

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### Abstract:

During a PCR-based screen of antibiotic resistance genes (ARGs) associated with integrons in saliva-derived metagenomic DNA of healthy human volunteers, two novel variants of genes encoding a D-alanine-D-alanine ligase (ddl6 and ddl7) located within gene cassettes in the first position of a reverse integron were identified. *Treponema denticola* was identified as the likely host of the ddl cassettes. Both ddl6 and ddl7 conferred high level resistance to D-cycloserine when expressed in *Escherichia coli* with ddl7 conferring four-fold higher resistance to D-cycloserine compared to ddl6. A SNP was found to be responsible for this difference in resistance phenotype between both ddl variants. Molecular dynamics simulations were used to explain the mechanism of this phenotypic change at the atomic level. A hypothesis for the selection of ddl containing integron gene cassettes is proposed, based on molecular docking of plant metabolites within the ATP and D-cycloserine binding pockets of Ddl.

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### Publication of speakers:

1. Rahman, Md & Kaiser, Frank & Jamshidi, Shirin & Rahman, Khondaker & Mullany, Peter & Roberts, Adam. (2020). Integron Gene Cassettes Harboring Novel Variants of D-Alanine-D-Alanine Ligase Confer High-level Resistance to D-Cycloserine. 10.1101/2020.05.09.085589.
2. Rafi, Md & Azad, Dewan & Bhattacharjee, Mridula & Rahman, Nikita & Mubin, Kazi & Rahman, Md & Hossain, Golam. (2020). A hospital-based study on complementary and alternative medicine use among diabetes patients in Rajshahi, Bangladesh. BMC Complementary Medicine and Therapies. 20. 10.1186/s12906-020-03021-3. ISRN pharmaceuticals 2011
3. Rahman, Md & Mullany, Peter & Roberts, Adam. (2017). Draft Genome Sequence of *Eggerthia cateniformis* Strain MAR1 Isolated from Saliva of Healthy Humans. Genome Announcements. 5. e00638-17. 10.1128/genomeA.00638-17.

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