The Structure of the ParC Subunit of Topoisomerase IV from *Streptococcus Pneumoniae*

Ivan Laponogov^a, Dennis Veselkov^a, Maninder Sohi^a, Xiao-Su Pan^b, Mark Fisher^b, Mark Sanderson^a, ^aThe Randall Centre, King's College London, London SE1 1UL, UK. ^bDept of Biochemistry&Immunology, St. George's Hospital Medical School, London SW17 0RE, UK. Email: ivan.laponogov@kcl.ac.uk

Topoisomerases relieve torsional stress in DNA within cells by breaking one or both strands of DNA, then either winding or unwinding the DNA helix, followed by strand closure.

TopoIV (whose subunits are encoded by *ParC* and *ParE*) is a decatenating enzyme that resolves interlinked daughter chromosomes following DNA replication.TopoIV uses a double-strand passage mode as does Gyrase (which controls DNA supercoiling by relieving topological stress arising from the translocation of transcription and replication complexes bound to DNA) by a different mechanism: Gyrase wraps DNA around itself, while TopoIV does not. The difference in DNA-wrapping between Gyrase and Topo IV contributes to their different functional roles within cells.

The ParC subunit of TopoIV has been crystallised in tetragonal and hexagonal forms. Analysis of the tetragonal crystals (diffracted significantly better than hexagonal ones) showed that they were internally twinned. Present in the crystal are two *1222* crystal lattices aligned in opposite directions and forming pseudo 4-fold symmetry.

The structure of ParC subunit was solved by Molecular Replacement using a model build on the basis of the homologous GyrA subunit from *E.coli*[1] (1AB4 deposited in the PDB) as a model. Analysis of packing of the protein molecules in the unit cell shows screw axes \parallel to *c*, going in opposite directions.

[1] Cabral J.H.M., Jackson A.P., Smith C.V., Shikotra N., Maxwell A., Liddington R.C., *Nature*, 1997, **388**, 903.

Keywords: topoisomerase IV, ParC, twinning