



	<b>Experiment title:</b> ISMB application, Birkbeck; School of Pharmacy & NPP, UCL; Biological and Chemical Sciences, Queen Mary College London. Kozielski group	<b>Experiment number:</b> MX1983
<b>Beamline:</b> ID23-2 ID30A-1 ID29 ID30A-3	<b>Date of experiment:</b> from: 23/04/2018 to: 24/04/2018 from: 30/06/2018 to: 01/07/2018 from: 12/07/2018 to: 13/07/2018 from: 1/12/2018 to: 02/12/2018	<b>Date of report:</b> 25/02/2019
<b>Shifts:</b> 12	<b>Local contact(s):</b> 23/4 N/A 30/06: Bowler M 12/07: De Sanctis D 1/12: Melnikov I	<i>Received at ESRF:</i>
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**Report:**

Frank Kozielski's group solved two structures of human Eg5 in complex with K858 (1). This structure provided a platform for structure-based drug design and was essential for rational design of inhibitor analogues. This work has recently been published.

We have developed a screen for the crystallisation of viral RNA-dependent RNA polymerases (RdRps) and confirmed its usefulness by solving two RdRp-inhibitor complexes of dengue virus RdRp (2). This work has recently been published.

Human MCAK structures in various nucleotide states have been solved and the structures are being prepared for submission. The manuscript is in preparation.

We have collected data on a large variety of crystals of *M. tuberculosis* FtsZ and DENV RdRp in complex with fragments. These structures will reveal novel inhibitors binding sites and will allow structure-based drug design (in progress). These complex structures will serve as a basis to develop

inhibitors with higher potency and efficacy. For example, data collected from the Massif beamtime for Dengue RdRp in complex with fragments (about 200 data sets) has been processed by standard methods but without any success, but the same data has been processed using the PanDDA software from DLS and a range of fragments binding to DENV RdRp has been identified.

#### **List of PDB submissions as a direct result of ESRF time**

6G6Y

6G6Z

#### **List of publications attributable to ESRF time**

1. Talapatra, S.K., Tham, C.L., Guglielmi, P., Cirilli, R., Chandrasekaran, B., Karpoormath, R., Carradori, S., Kozielski, F. **(2019)**. Crystal structure of the Eg5 - K858 complex and implications for structure-based design of thiadiazole-containing inhibitors. *Eur. J. Med. Chem.* **156**, 641-651.

2. Riccio, F., Talapatra, S.K., Oxenford, S., Angell, R., Mazzon, M., Kozielski, F. **(2019)**. Development and validation of RdRp Screen, a crystallization screen for viral RNA-dependent RNA polymerases. *Biol Open* Jan 2;8(1).

