Research Highlights

Canadian Macromolecular Crystallography Facility

The CMCF is truly a national facility, with users from all across the country collecting data either in person, remotely, or through the Mail-In program. CMCF users from both Canada and abroad have been making an impact on the international crystallographic landscape since 2006, using data from the CMCF for over 150 publications and over 250 deposits to the Protein Data Bank, and counting...

Highlights of Recent Publications Based on Data Collected at the CMCF...

- C. Calmettes, J. Alcantara, R.H. Yu, A.B. Schryvers and T.F. Moraes. (2012). The structural basis of transferrin sequestration by transferrin-binding protein B. ***Nat. Struct. Mol. Biol.*** 19(3), 358-360
- V.J. O'Sullivan, I. Barrette-Ng, E. Hommema, G.T. Hermanson, M. Schofield, S.-C. Wu, C. Honetschlaeger, K.K.-S. Ng, S.-L. Wong. (2012). Development of a tetrameric streptavidin mutein with reversible biotin binding capability: engineering a mobile loop as an exit door for biotin. ***PLoS ONE*** 7(4), e35203
- M.F. Sarhan, C.C. Tung, F. Van Petegem and C.A. Ahern. (2012). Crystallographic basis for calcium regulation of sodium channels. ***Proc. Natl. Acad. Sci. U.S.A.*** 109(9), 3558-3563
- A.C.Y. Yu, L.J. Worrall and N.C.J. Strynadka. (2012). Structural insight into the bacterial mucinase StcE essential to adhesion and immune evasion during enterohemorrhagic *E. coli* infection. ***Structure*** 20, 707-717
- T.W. James, N. Frias-Staheli, J.P. Bacik, J.M. Levingston Macleod, M. Khajehpour, A. Garcia-Sastre and B.L. Mark. (2011). Structural basis for the removal of ubiquitin and interferon-stimulated gene 15 by a viral ovarian tumor domain-containing protease. ***Proc. Natl. Acad. Sci. U.S.A.*** In Press
- U. Kanjee, I. Gutsche, E. Alexopoulos, B. Zhao, M. El Bakkouri, G. Thibault, K. Liu, S. Ramachandran, J. Snider, E.F. Pai and W.A. Houry. (2011). Linkage between the bacterial acid stress and stringent responses: the structure of the inducible lysine decarboxylase. ***EMBO J.*** 30(5), 931-944
- S. Quan, P. Koldewey, T. Tapley, N. Kirsch, K.M. Ruane, J. Pfizenmaier, R. Shi, S. Hofmann, L. Foit, G. Ren, U. Jakob, Z. Xu, M. Cygler and J.C. Bardwell. (2011). Genetic selection designed to stabilize proteins uncovers a chaperone called Spy. ***Nat. Struct. Mol. Biol.*** 18(3), 262-269
- R. Shi, L. McDonald, Q. Cui, A. Matte, M. Cygler and I. Ekiel. (2011). Structural and mechanistic insight into covalent substrate binding by *Escherichia coli* dihydroxyacetone kinase. ***Proc. Natl. Acad. Sci. U.S.A.*** 108(4), 1302-1307
- M.L. Tonkin, M. Roques, M.H. Lamarque, M. Pugniere, D. Douguet, J. Crawford, M. Lebrun and M.J. Boulanger. (2011). Host cell invasion by apicomplexan parasites: insights from the co-structure of AMA1 with a RON2 peptide. ***Science*** 333, 463-467
- S.J. Campbell, R.A. Edwards and J.N.M. Glover. (2010). Comparison of the structures and peptide binding specificities of the BRCT domains of MDC1 and BRCA1. ***Structure*** 18 (2), 167-176
- X. He, P. Szewczyk, A. Karyakin, M. Evin., W.X. Hong, Q. Zhang and G. Chang. (2010). Structure of a cation-bound multidrug and toxic compound extrusion transporter. ***Nature*** 467, 991-994
- M.Q. Khan, B. Sweeting, V.K. Mulligan, P.E. Arslan, N.R. Cashman, E.F. Pai and A. Chakrabartty. (2010). Prion disease susceptibility is affected by β-structure folding propensity and local side-chain interactions in PrP. ***Proc. Natl. Acad. Sci. U.S.A.*** 107, 19808-19813
- A.L.Lovering, L.Y-C Lin, E.W. Sewell, T.Spreter, E.D. Brown, N.C.J. Strynadka. (2010). Structure of the bacterial teichoic acid polymerase TagF provides insights into membrane association and catalysis. ***Nat. Struct. Mol. Biol.*** 17 (5), 582-589
- K.L. Peña, S.E. Castel, C. de Araujo, G.S. Espie and M.S. Kimber. (2010). Structural basis of the oxidative activ-ation of the carboxysomal gamma-carbonic anhydrase, CcmM. ***Proc. Natl. Acad. Sci. U.S.A.*** 107 (6), 2455-2460
- R. Shi, A. Proteau, M. Villarroya, I. Moukadiri, L. Zhang, J.-F. Trempe, A. Matte, M.E. Armengod, M. Cygler. (2010). Structural basis for Fe-S cluster assembly and tRNA thiolation mediated by IscS protein-protein interactions. ***PLoS Biology*** 8 (4), e10000354
- C.C. Tung, P.A. Lobo, L. Kimlicka and F. Van Petegem. (2010). The amino-terminal disease hotspot of ryanodine receptors forms a cytoplasmic vestibule.. ***Nature*** 468, 585-588

For more Info:

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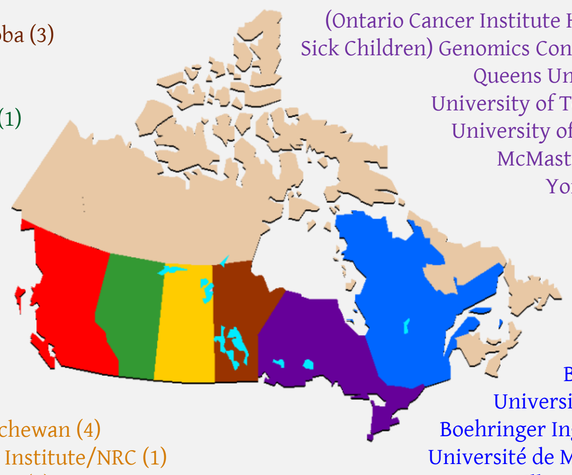
Macromolecular Crystallographers in Canada



University of Manitoba (3)

Univ. of Lethbridge (1)
Univ. of Alberta (5)
Univ. of Calgary (3)

Simon Fraser (4)
Univ. of Victoria (3)
UBC (7)

University of Saskatchewan (4)
Plant Biotechnology Institute/NRC (1)
Canadian Light Source (3)

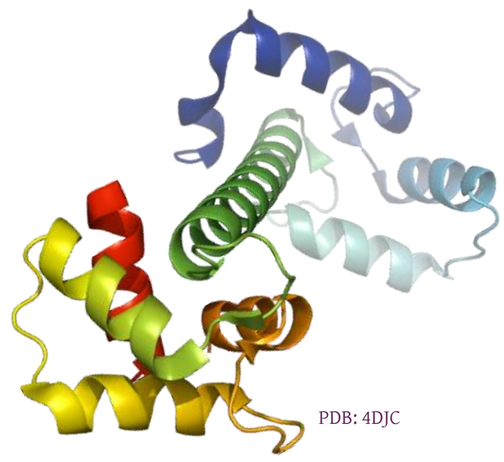
(Ontario Cancer Institute Hospital for Sick Children) Genomics Consortium (3)
Queens University (3)
University of Toronto (10)
University of Guelph (2)
McMaster Univ. (3)
York Univ. (2)
UWO (2)

BRI/NRC (1)
Université Laval (1)
Boehringer Ingelheim (2)
Université de Montréal (1)
McGill University (4)

In an effort to support up-and-coming Canadian crystallographers, the CMCF hosts the Annual CLS Mx Data Collection School, an intense five-day program designed to give participants a breadth of practical abilities and a depth of knowledge, equipping them to effectively collect and process data independently.

The CMCF supports an active Canadian and international user base, playing a key role in exciting experiments like these every day...

How Does Calcium Regulate the Heartbeat?



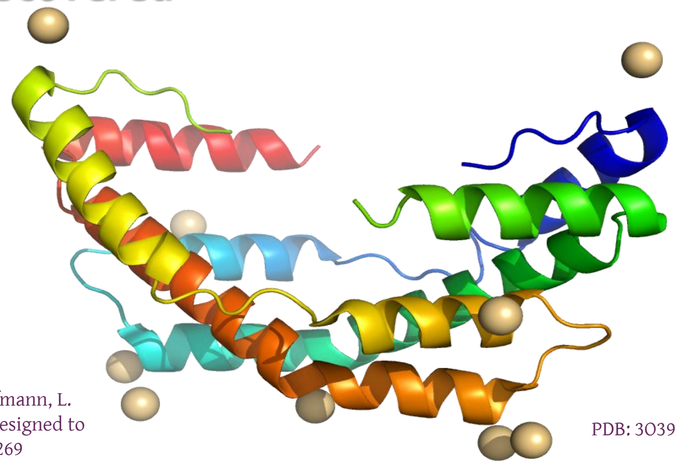
PDB: 4DJC

Brugada syndrome is a disease characterised by an increased risk of sudden cardiac death. Properly-functioning sodium channels are critical to the normal contraction and relaxation of heart muscle cells. Calcium ions bound to another protein called calmodulin can modulate these channels. Researchers have solved the structure of calcium-bound calmodulin in complex with the inactivation gate of a sodium channel. Several mutations near the calmodulin binding site have been identified which result in arrhythmias such as Brugada syndrome.

M.F. Sarhan, C.C. Tung, F. Van Petegem and C.A. Ahern. (2012). Crystallographic basis for calcium regulation of sodium channels. *Proc. Natl. Acad. Sci. U.S.A.* 109(9), 3558-3563

New Class of Chaperone Protein Discovered

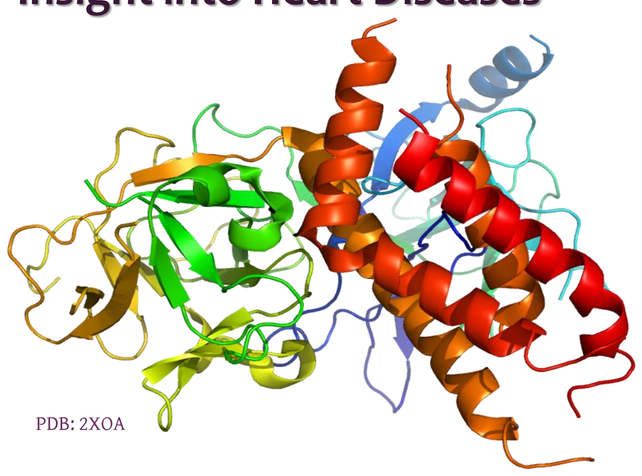
Chaperone proteins make possible the correct folding of other protein molecules in the cell. Researchers have induced bacteria to over-produce a periplasmic chaperone protein called Spy. These unique cradle-shaped dimers help protein refolding and suppress protein aggregation independently of ATP.



S. Quan, P. Koldewey, T. Tapley, N. Kirsch, K.M. Ruane, J. Pfizenmaier, R. Shi, S. Hofmann, L. Foit, G. Ren, U. Jakob, Z. Xu, M. Cygler and J.C. Bardwell. (2011). Genetic selection designed to stabilize proteins uncovers a chaperone called Spy. *Nat. Struct. Mol. Biol.* 18(3), 262-269

PDB: 3O39

Insight into Heart Diseases



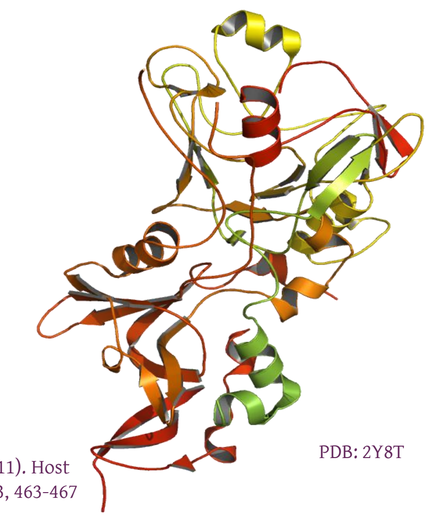
PDB: 2XOA

Genetic variation in ryanodine receptor 'hotspots' can play a role in diseases affecting muscles, including congenital heart disease. Researchers from the University of British Columbia have combined crystallographic data obtained at beamline 08ID-1 and the Stanford Synchrotron Radiation Lightsource with electron microscopy data to shed light on amino-terminal ryanodine receptor disease hotspot.

C.C. Tung, P.A. Lobo, L. Kimlicka and F. Van Petegem. (2010). The amino-terminal disease hotspot of ryanodine receptors forms a cytoplasmic vestibule.. *Nature* 468, 585-588

Exposing the Secret Lives of Parasites

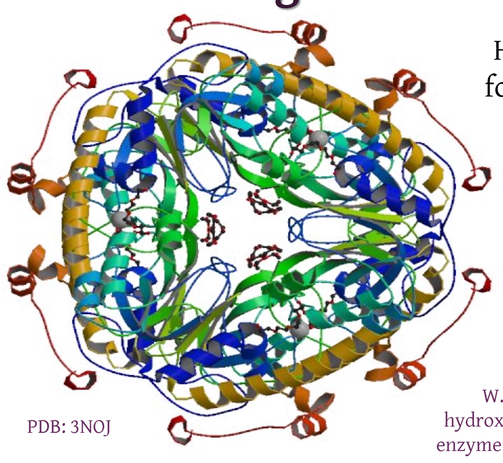
Toxoplasma and *Plasmodium* parasites cause numerous diseases worldwide, including malaria and toxoplasmosis. Interestingly, these parasites attack host cells in a very active manner, providing the receptor for binding to the host cell. Interaction thus occurs through a protein called AMA1 to a rhoptry neck (RON) complex provided by the parasite and injected into the host cell. Now researchers have used data collected at the CMCF to determine the structure of AMA1 with a RON2 peptide to give insight into this interaction.



PDB: 2Y8T

M.L. Tonkin, M. Roques, M.H. Lamarque, M. Pugniere, D. Douguet, J. Crawford, M. Lebrun and M.J. Boulanger. (2011). Host cell invasion by apicomplexan parasites: insights from the co-structure of AMA1 with a RON2 peptide. *Science* 333, 463-467

Understanding Pollutant Degradation by Bacteria



PDB: 3NOJ

HMG/CHA aldolase from *Pseudomonas putida* is part of a larger pathway for breaking down harmful components of fossil fuel pollution and coal derivatives (fluorene and its analogues) and substances found in plastics and pesticides (phthalate isomers). Researchers have grown crystals of the enzyme and solved the crystal structure in order to better understand how the active site is organized. This has allowed them to propose a catalytic mechanism based on the structural features, kinetics and information available about related aldolases.

W. Wang, S. Mazurkewich, M.S. Kimber and S.Y.K. Seah. (2010). Structural and kinetic characterization of 4-hydroxy-4-methyl-2-oxoglutarate / 4-carboxy-4-hydroxy-2-oxoadipate aldolase, a protocatechuate degradation enzyme evolutionarily convergent with the HpaI and DmpG pyruvate aldolases. *J. Biol. Chem.* 285(47), 36608-36615

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