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Recent breakthroughs in the field of cryo-electron microscopy (cryo-EM) provide new prospects for determination of the structures of a variety of macromolecular assemblies and offer unprecedented opportunities for drug discovery. The prospect that the determination of protein structures to atomic resolution will no longer be limited by size, or by the need for crystallization represents a significant and exciting horizon in structural biology. I will discuss the application of these methods to analyze structures of a variety of biologically and medically relevant multi-protein complexes and membrane protein assemblies, which have historically represented the most challenging frontier in structural biology.

Selected publications:

- Merk A., Bartesaghi A, Banerjee S, Falconieri V, Rao P, Davis M, Pragani R, Boxer M, Earl LA, Milne JLS, Subramaniam S (2016) Breaking cryo-EM resolution barriers to facilitate drug discovery. *Cell*, 165 1698-1707.
- Matthies D, Dalmas, O, Borgnia, MJ, Dominik, PK, Merk, A, Rao, P, Reddy, BG, Islam, S., Bartesaghi, A, Perozo, E, Subramaniam, S (2016) Cryo-EM Structures of the Magnesium Channel CorA Reveal Symmetry Break Upon Gating. *Cell*, 164, 747-756.
- Banerjee, S, Bartesaghi, A, Merk, A, Rao, P, Bulfer, SL, Yan, Y, Green, N, Mroczkowski, B, Neitz, RJ, Wipf, P, Falconieri, V, Deshaies, RJ, Milne, JLS, Hury D, Arkin, M, Subramaniam S (2016) 2.3 Å resolution cryo-EM structure of human p97 and mechanism of allosteric inhibition. *Science*, 351,871-875.
- Meyerson JR, Chittori S, Merk A, Rao P, Han TH, Serpe, M, Mayer ML, Subramaniam S (2016) Structural basis of kainate subtype glutamate receptor desensitization. *Nature* 537:567-571.
- Bartesaghi A, Merk A, Banerjee S, Matthies D, Wu X, Milne JLS, Subramaniam S (2015) 2.2 Å resolution cryo-EM structure of  $\beta$  -galactosidase in complex with a cell-permeant inhibitor. *Science* 348:1147-1151.