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“Cpx-dependent sensing and adaptation to adhesion”

Wed. Oct. 21, 2015
MCKN 031 @ 2:30 pm

The status of the bacterial envelope is monitored and controlled partly by the sensor kinase CpxA and the response regulator CpxR. CpxA can be activated by adhesion to abiotic surfaces via the outer membrane lipoprotein NlpE, resulting in elevated phosphorylated CpxR (CpxR~P). CpxR~P changes the expression of hundreds of genes that include chaperones and proteases together with inner membrane proteins involved in transport/efflux, metal homeostasis, and respiration. How NlpE and CpxA jointly sense adhesion and why this requires up-regulation of Cpx-regulated genes are unknown. We used genetic analyses to characterize the surface-sensing mechanisms used by NlpE and the roles of Cpx-regulated genes. We show that the carboxyl terminal domain of NlpE and the connecting flexible linker are important for signalling CpxA. NlpE may act as part of a larger protein complex to sense adhesion, since mutation of the genes encoding other envelope-localized proteins negates activation of CpxA by NlpE and NlpE physically associates with some of these gene products. We solved the crystal structure of the sensing domain of CpxA and mapped mutations affecting activity of the sensor kinase onto the structure to show that activation of the Cpx response likely involves the disruption of a PDC (PhoQ-DcuS-CitA) domain in CpxA that disrupts phosphatase activity. Induction of the Cpx response leads to direct down-regulation of respiratory complexes and elimination of these complexes can suppress the toxicity of Cpx inducing signals when *cpxR* is mutated. Altogether our data suggest that CpxA senses extracellular signals through envelope spanning protein assemblies and that down-regulation of respiratory complexes is an important mechanism of adaptation. These events are likely important in the intestine, since *cpx* mutants exhibit severe growth phenotypes under conditions that mimic this environment.

Fall 2015 Schedule

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| Oct. 7th | Dr. Michael Moran, University of Toronto and Hospital for Sick Children (Host: Dr. N. Jones) |
| Oct. 21st | Dr. Tracy Raivio, University of Alberta (Host: Dr. C. Whitfield) |
| Nov 4th | Dr Rheal Towner, Oklahoma Medical Research Foundation (Host: Dr. D. Josephy) |
| Nov 18th | Dr. David Evans, University of Alberta (Host: Dr. P. Krell) |

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* ALL WELCOME TO ATTEND *

* COFFEE, TEA AND TIMBITS *

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