

**W0174**

**Structural Mechanism of Carbon Catabolite Repression.** Richard G. Brennan, Dept. of Biochemistry & Molecular Biology, Oregon Health & Science Univ., Portland, OR 97239.

Regulation of transcription often requires the binding of a small molecule to the regulator or reversible chemical modification of the regulator in order to effect its repressor or activator function. However, small molecule binding and chemical modification are not the only mechanisms utilized to regulate transcription. In Gram positive bacteria, regulation of the genes involved in carbon catabolite repression (CCR) requires the LacI/GalR family member, CcpA to bind to a second protein, HPr, which has been phosphorylated on residue serine 46 (Ser46P). This complex can then bind *cre* DNA sequences to either repress or activate the numerous genes involved in carbon catabolism. HPr can also be phosphorylated on residue His15 and in this state is a critical intermediate in the PTS sugar uptake pathway. Because CCR and PTS are competing pathways, it is logical that HPr(His15P) inhibits CCR and HPr(Ser46P) interferes with the PTS. To understand the allosteric mechanism of the integrated control of carbon catabolite repression and the PTS pathway, we have determined the structure of a CcpA-HPr(Ser46P)-DNA ternary complex to 2.80 Å resolution and the structure of CcpA in the absence of corepressor to 2.75 Å resolution. These results will be presented.