Title:	Molecular insights into effector binding by DgoR, a GntR/FadR family transcriptional repressor of D-galactonate metabolism in Escherichia coli
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Abstract:	Several GntR/FadR transcriptional regulators govern sugar acid metabolism in bacteria. Although effectors have been identified for a few sugar acid regulators, the mode of effector binding is unknown. Even in the overall FadR subfamily, there are limited details on effector-regulator interactions. Here, we identified the effector-binding cavity in Escherichia coli DgoR, a FadR subfamily transcriptional repressor of D-galactonate metabolism that employs D-galactonate as its effector. Using a genetic screen, we isolated several dgoR superrepressor alleles. Blind docking suggested eight amino acids corresponding to these alleles to form a part of the effector-binding cavity. In vivo and in vitro assays showed that these mutations compromise the inducibility of DgoR without affecting its oligomeric status or affinity for target DNA. Taking Bacillus subtilis GntR as a representative, we demonstrated that the effector-binding cavity is similar among FadR subfamily sugar acid regulators. Finally, a comparison of sugar acid regulators with other FadR members suggested conserved features of effector-regulator recognition within the FadR subfamily. Sugar acid metabolism is widely implicated in bacterial colonization and virulence. The present study sets the basis to investigate the influence of natural genetic variations in FadR subfamily regulators on their sensitivity to sugar acids and ultimately on host-bacterial interactions.
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