[MS5–02] The molecular basis of phosphate discrimination in arsenate-rich environments.

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Arsenate and phosphate are abundant on our planet and exhibit tremendous similarities: nearly identical pKa values, similarly charged oxygen atoms, and thermochemical radii that differ by only 4%. However, phosphate is indispensable whereas arsenate is toxic. This observed extensive similarity raises the question whether arsenate may substitute for phosphate in certain niches [1]. Whether it is used or excluded, discriminating phosphate from arsenate is a paramount challenge: enzymes that utilize phosphate are indeed unable to discriminate these two anions. This is one of the main reasons for the high toxicity of arsenate. Can proteins discriminate between these two anions, and how would they do so?

We focussed on the cellular phosphate uptake mechanism that faces this challenge, especially in arsenate-rich environments. More precisely, we examined the periplasmic Phosphate-Binding Proteins (PBPs) of the ABC-type transport system that mediates phosphate uptake into bacterial cells. We were able to show that all tested PBPs can efficiently discriminate phosphate over arsenate by at least 500-fold [2]. We have solved the structure of one of these PBPs, bound with phosphate and arsenate, at sub-Ångstrom resolutions (0.88-0.98Å). Both anions are bound and immobilized by a constellation of dipole-anion interactions and repulsive interactions. This binding mode is responsible for the 4% larger arsenate distorting a short, unique, Low-Barrier Hydrogen Bond (LBHB) [2]. These structural determinants enable the phosphate transport system to bind phosphate selectively over arsenate (at least 103 excess) even in highly arsenate-rich environments such as the Mono Lake (California, USA).

[1] Wolfe-Simon *et al., Science.* 2011, **332**, 1163-6.
[2] Elias *et al., Nature*. 2012, **491**, 134-7.

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