结构和构象动力学的假单胞菌Aeruginosa毒素，ExoU

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假单胞菌Aeruginosa是机会性病原菌，特别是在免疫缺陷患者、烧伤患者和患有囊性纤维化的人群中。A. aeruginosa产生类型III毒素的菌株特别具有致病性。我们以前已经证明ExoU是一种磷脂酶，它需要超氧化物歧化酶(SOD)作为宿主细胞因子。这种对宿主细胞的依赖性防止了ExoU对宿主细菌的损害。我们使用定点自旋标记(DDSL)来研究重组ExoU的结构动力学。常规EPR研究表明，ExoU与SOD和脂质体的相互作用导致催化活性位点周围区域的移动性增加。DEER实验表明，与SOD的相互作用导致ExoU的C端域从活性位点移动约9 Å。这些结果为ExoU的激活所需的构象变化提供了见解，并表明了一种保守的与宿主磷脂酶作用机制。

Pseudomonas aeruginosa is an opportunistic pathogen of particular importance in immunocompromised patients, burn patients, and individuals with cystic fibrosis. P. aeruginosa strains that produce the type III toxin, ExoU, are especially virulent. We have previously shown that ExoU is a phospholipase that requires superoxide dismutase (SOD) as a eukaryotic cofactor. The requirement of a eukaryotic cofactor prevents ExoU from damaging the host bacterium. We have used site-directed spin labeling (SDSL) to examine the structural dynamics of recombinant ExoU. Conventional EPR studies show increased mobility in the region surrounding the catalytic site upon interaction with SOD and substrate liposomes. DEER experiments indicate that interaction with SOD causes a C-terminal domain of ExoU to be displaced away from the active site by ~ 9 Å. These results provide insight into conformational changes required for ExoU activation, and suggest a conserved mechanism of action with eukaryotic phospholipases.