Most microbes have on the order of 1000-2000 enzymes, and probably all have additional secondary activities that are physiologically irrelevant. The number of promiscuous activities in any proteome is unknowable, but undoubtedly large. If we assume even a modest number of 10 promiscuous activities per enzyme, there could be as many as 10,000 – 20,000 promiscuous activities lurking in the proteome. These promiscuous activities may cause some "leakiness" in the metabolic network that normally does not impact fitness. However, when a microbe needs to evolve a new metabolic pathway – for example, to degrade a new source of carbon or synthesize a metabolite that was previously available in the environment – these promiscuous activities can be patched together to generate new pathways that we term "serendipitous". We are studying the potential for assembly of serendipitous pathways in a model system in which we have blocked the pathway for synthesis of the essential cofactor pyridoxal 5-phosphate (PLP) by deleting *pdxB* in *E. coli*. By supplying an intermediate in a previously identified serendipitous pathway in M9/glucose medium, we can evolve strains that have recovered robust growth using primarily that pathway to make PLP. Prolonged adaptation in M9/glucose alone also results in strains that have restored robust growth, but these strains make PLP by a different serendipitous pathway. Further, the patterns of mutations we observe in adapted strains differ depending upon whether the concentration of glucose is 0.4% or 0.2%. These results demonstrate that 1) there are many untapped resources for metabolic innovation lurking in the proteome of *E. coli*; and 2) the most accessible solution to a metabolic challenge depends strongly on the environmental conditions.