HisA mutants are like screws in cars: what is similar, is not the same

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Every living organism has their specific features, which make them distinguishable and unique. The hair and eye color, the height, the shape of the body and a million other parameters define that a human being is not an ape or a snail, but a human being. For a bacterium, it is more the ability to produce certain molecules they need in order to survive that distinguishes them. But one thing is common in a bacterium, a snail or a human being: every feature is the result of proteins, molecules that enable your body to work as it does.

Let's scale up a bit with an analogy. Say that a car factory is a tiny bacterium. In our imaginary factory cars from the size of a toy up the huge trucks are produced: with different shapes, sizes and functions. This factory also produces cars, which help the factory itself to work. Moreover, there are no humans working by the conveyor belts, but cars. Now imagine that a bacterium works like that just replace the cars with proteins. As cars make cars from sketches in our factory, proteins make proteins from sketches in a bacterium.

In my master thesis, I was interested in one 'car' working next to a 'conveyor belt'. This conveyor belt in the bacterium is the production of a molecule, called histidine, and the car in the bacterium is called HisA. As at a conveyor belt, there are several steps from the start to the finish in the production of a molecule. Our HisA 'car' is able to do only one step of the production. But there is another conveyor belt, producing another molecule, called tryptophan, running parallel to the histidine production. A 'car' called TrpF works by that belt among others. This TrpF is interesting, because HisA has the chance to replace it if it goes wrong or is absent. All you have to do is just reshape HisA a bit. For the bacterium, shaping means to introduce mutations in its protein.

There are many HisAs reshaped for having TrpF activity, two of which I have been working with. One of them, call it 'A' is very clumsy when it has to replace TrpF, although very good in its own job, whereas the other, call it 'F' has already forgotten its original task by the histidine production belt but does a decent job in replacing TrpF. Interestingly, these HisA mutants are extremely similar in shape, but in function they are the opposites of each other.

First, I was trying to teach the 'A' mutant how to do the TrpF job better by introducing a new mutation, and second, I have compared 'A' and 'F' mutants in shape and function, by making 'B', 'C', 'D' and 'E' mutants.

HisA mutant 'A' seemed to be so clumsy in the TrpF job that the mutation I introduced did not improve it at all. On the other hand 'B', 'C', 'D' and 'E' mutants pointed out a difference between 'A' and 'F', which is as big as an atom. In the car analogy, it is like a difference between an 8 mm screw and a 10 mm screw: close to nothing but still a lot.

In molecular biology this result is very important for its lesson about tiny changes that can radically change the function of a protein.

Degree project in Biology, Master of Science (2 years), 2016

Examensarbete i biologi 45 hp till magisterexamen, Uppsala Universitet, 2016

Biology Education Center and Department of Cell and Molecular Biology

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