TwistDx™ blog

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TwistDx: A history of science, serendipity and success

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TwistDx Insights

The curious aspect of scientific research is that you never know where it will lead you. TwistDx started 18 years ago – back then it was ASM Scientific – and we could not have predicted that we would find ourselves pioneering the use of RPA in 2017. A mix of good ideas, circumstances, and trial and error have led us to where we are today, and will no doubt continue to accompany our future success.

Aiming in a different direction

Not everyone knows that TwistDx was set up to explore an idea for single molecule sequencing, rather than DNA amplification and detection. One of the tasks was finding a mechanism to create defined ends in small fragments of target DNA, which could then serve as sites for the assembly of the enzymatic sequencing complex. This complex challenge sparked the idea of using a mixture of synthetic oligonucleotides and recombination proteins, and it quickly became apparent that – if we used two priming oligonucleotides which opposed each other on the target DNA – we could build a mechanism for exponential amplification.

Copying nature

Back in 2003, the single molecule sequencing space became overcrowded by bigger companies and investors, and we made the decision to concentrate on RPA and DNA amplification. The key to our success is mimicking the recombination system that exists in T4-like bacteriophages, consisting of three proteins: a recombinase called UV-sensitive X (uvsX), Gp32 – which is a single-strand DNA-binding protein – and another small peptide called uvsY. These proteins had been discovered decades earlier as part of mutagenesis screens, and they were well characterised by the time we started working with them. However, no one had used them as we planned to.

The missing ingredient

Attempting to recreate the recombination system and combining it with a strand-displacing DNA polymerase required a lot of trial and error, and a key development was including certain additives, such as the crowding agent polyethylene glycol (PEG). We reasoned that crowding agents increase the local concentration of our active ingredients, facilitating the recombination and primer extension events. We tried many different agents with various molecular weights and concentrations, and eventually hit on the combination that gave us the signals we were looking for.

Serendipity

Much like other scientific research, our success was a combination of informed decision-making and serendipity. Even armed with our knowledge of the recombination system, we could not have anticipated the extraordinary accelerating effect of a crowding agent! Once we had established the bones of the amplification, we worked on developing different modes of detection, such as the fluorophore quencher probes.

By 2006, we were ready to publish our first paper on RPA, and we turned our attention to finding applications that could benefit from our technology. And that is what excites us today. RPA is now established as a rapid, effective technique for DNA amplification, and the next phase of RPA's history will be written in partnership with our customers, who continue to discover fascinating applications for our technology.