IN RECENT DECADES, most pharmaceutical companies have stopped investing in drug discovery for psychiatric diseases, such as schizophrenia, due to low profitability. Consequently, the drug pipeline has dried up and many symptoms of psychiatric diseases cannot be effectively treated.

Dr Michael Wehr and his team at Ludwig Maximilian University of Munich, Germany, have been investigating new ways to modulate activities of drug targets in schizophrenia. One factor that Wehr focuses on is the nature of interactions between Neuregulin 1 (a signalling factor) and membrane receptor ErbB4 – interactions that are linked to higher risk for schizophrenia.

SPLIT UP AND LOOK FOR CLUES

Wehr and colleagues realised that they needed better tools to investigate this and similar protein-protein interactions. They therefore developed a genetically encoded biosensor that is based on the split tobacco etch virus (TEV) system.

The system encodes fragments of the TEV protease fused to protein interaction partners. When the interacting proteins are expressed in living cells, the TEV protease fragments are attached. Subsequently, when the two proteins interact, the TEV protease fragments reassemble and form an active protease. The protease activity is then converted to a measurable readout, such as luminescence.

Importantly, this technique is applicable to various readout systems and protein-protein interactions. It can also be used to set up high throughput assays, which are frequently used to identify new drug ‘hits’. Furthermore, the TEV system can be combined with a multi-parametric reporter assay format, termed EXT assay, to profile target specificities and compound actions in living cells. The value of the split TEV system and the EXT assay technologies are such that they were patented and later commercialised by Munich-based company SYSTASY Bioscience – a company of which Wehr is both co-founder and shareholder.

FILLING THE INNOVATION GAP FROM BENCH TO BEDSIDE

Wehr and his team in Munich are already applying the split TEV system to identify new drugs for schizophrenia treatment. Using the TEV system to study the effect of drug candidates on the neuregulin 1-ErbB4 interaction, the team has found one particularly promising drug that could be repurposed as an ‘add-on’ therapy for schizophrenia.

By trialling drugs that are already approved by the US Food and Drug Administration (FDA), ie. by drug repurposing, Wehr hopes that he can stimulate activities for the schizophrenia drug discovery pipeline. Moreover, his approach advocates collaborations between academia and industry for supporting the pharmaceutical industry in discovering drugs to treat less profitable disease targets. This way, Wehr also envisions a smaller gap from bench to bedside.