

could have a myriad of applications in synthetic biology. However, designing new proteins that selectively interact and that can assemble *in vivo* requires the design of two components that interact in a way that is orthogonal to the numerous motifs found within cells — a task which is far from easy.

A team led by Lynne Regan at Yale University have now engineered three different protein–peptide interactions that are not found in nature. They based their systems on the tetratricopeptide repeat affinity protein (or TRAP), which binds peptides made of five amino acids with both high affinity and selectivity. To develop a range of unique interactions the team introduced mutations to the binding pocket of the TRAP protein along with corresponding mutations to the peptide sequence. The mutations were designed to alter the size of the hydrophobic amino acid at the C-terminus of the peptide, along with the corresponding binding pocket; and to alter the charge at positions two and three in the peptide along with complementary alterations made to the protein. This led to the development of three different TRAP proteins that bound to their respective partner peptides, but showed low cross-reactivity to the partners of other TRAP proteins. The team also showed that they could tune the strength of one TRAP–peptide interaction by mutating the tryptophan amino acid at the C-terminus of the peptide to a smaller hydrophobic amino acid.

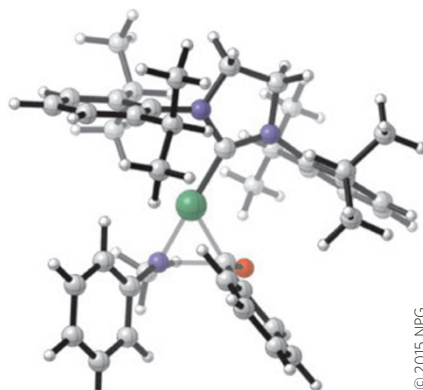
Next the team investigated whether the TRAPs could bind their partner peptides inside living cells. Experiments using *Escherichia coli* cell lysate showed that the TRAP–peptide interaction was not inhibited by the cellular proteins within *E. coli* and, crucially, a fluorescence assay proved that the TRAPs did bind their partner peptides inside *E. coli* cells. Preliminary experiments also indicate that the TRAP–peptide interaction should also assemble in mammalian and yeast cells. RJ

#### NICKEL CATALYSIS

### Amide activation

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The canon of synthetic chemistry has it that amides are relatively unreactive. This is usually explained by invoking resonance stabilization in which the nitrogen lone pair is donated into the anti-bonding ( $\pi^*$ ) orbital of the carbonyl, reducing its electrophilicity. This stability means that substrates containing amides can often be carried through multistep syntheses without significant concern. The amide



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bond is also the key structural component of proteins and yet nature is able to break them with ease using enzymes. Now, a team led by Neil Garg from the University of California, Los Angeles have developed a nickel-catalysed procedure for the conversion of amides to esters.

In line with the known stability of amides, previous approaches to this type of transformation have required the use of harsh acidic or basic conditions and a large excess of alcohol nucleophile — often used as reaction solvent. And, although metal-catalysed activation of carbon–heteroatom bonds in other carbonyl compounds has been reported, activation of the C–N bond in amides has not. Building upon their prior work on the activation of strong aryl–heteroatom bonds, Garg and co-workers turned to nickel catalysis. They began their study by performing density functional theory calculations to determine both the free-energy change for the methanolysis of a variety of *N*-substituted benzamides, and also the activation barrier for oxidative addition of the amide to an *N*-heterocyclic carbene–nickel catalyst. The calculations suggested that methanolysis of *N*-methyl-*N*-phenylbenzamides would be favourable both thermodynamically and kinetically and this was borne out experimentally — with the reaction producing an excellent yield of ester using only a small excess of methanol at just 80 °C.

Garg and co-workers also showed that their reaction conditions were applicable to a variety of electron-rich aryl, electron-poor aryl and heteroaryl amides, and that complex and sterically hindered alcohols could be used as nucleophiles. As it stands, however, reactions with alkyl amides have not been successful — though this also presents an opportunity for the chemoselective reaction of one amide in the presence of another. SD

Written by Enda Bergin, Stephen Davey, Thomas Faust and Russell Johnson.

## blogroll

### Better online science

Pictures taken in a lab and pictures of far-away worlds underpin great examples of scientific communication.

As scientists, we all strive to be better at communicating our work. Paige Jarreau at From the Lab Bench explains this very succinctly in her post about a talk she attended on scientific story telling (<http://go.nature.com/6OkhMi>). The Picture it... Chemistry blog goes into more detail with a step-by-step guide on how to write a science blog post (<http://go.nature.com/YoPdZk>). This fits with Laboratory News' newly launched Shout It Out service (<http://go.nature.com/BX8t4a>) which aims to encourage scientists to start shouting about their science — even if they don't have their own blog.

But science communication is not always about sharing your own work — sometimes it's about discussing and better communicating other popular science. Nowhere was this more important than the recent flyby of Pluto, as eloquently explained by Phil Plait at Bad Astronomy (<http://go.nature.com/kBIAOY>). And to help fill in some of the details for non-astronomers, C. C. Petersen at TheSpacewriter's Ramblings prepared a great primer on planetary geology (<http://go.nature.com/qggX6c>) to help explain Pluto's apparent geological activity.

Finally, there are some excellent examples of communicating science via YouTube. Maren Hunsberger's superb video series at Lunchbox Science has recently tackled 'How fire works' (<http://go.nature.com/1LKK5Q>). The very popular Vsauce3 takes time to try and explain the real physical implications of being Ant-Man (<http://go.nature.com/BrPxd>). And Tom Scott teams up with Robert Llewellyn to try and answer 'Are batteries heavier when they're full?' (<http://go.nature.com/rHMbah>). Even if we might already know the answers, these videos show how we can make science more engaging.

Written by Matthew Partridge, who blogs at <http://errantscience.com> and tweets as @MCeeP