**Bacteria shed light on new drug targets for inherited cancers**

## Scientists have succeeded in purifying a protein found in bacteria that could reveal new drug targets for inherited breast and ovarian cancers as well as other cancers linked to DNA repair faults.

## The study is published in the journal Nature.

The team, based at The University of Manchester’s Paterson Institute for Cancer Research and the Manchester Interdisciplinary Biocentre, are the first to decipher the structure of a protein called PARG – which plays an important role in DNA repair and acts in the same pathway as PARP.

PARP inhibitors have been showing great promise in clinical trials for patients with breast, ovarian and prostate cancers caused by mutations in genes called BRCA1 and BRCA2.

They work by blocking the action of PARP – a protein that chemically tags areas of DNA damage to highlight them to the cell’s DNA repair machinery.

PARG removes these chemical tags after the DNA damage has been repaired.

So the researchers believe that, similar to PARP inhibitors, drugs designed to block the action of PARG could be effective in treating cancer.

Lead author Dr Ivan Ahel, based at the Cancer Research UK-funded Paterson Institute, said: “For decades scientists have wanted to find out the structure of PARG, but its large size makes it very hard to produce in the lab.

By studying a smaller version of PARG found in bacteria, we’ve been able to create a ‘3D map’ that researchers can use to understand more about how PARG works.

The next step will be to investigate whether drugs that block its activity might be an effective way of treating cancers driven by faults in DNA repair genes.”

Co-author Professor David Leys, who is based in the Faculty of Life Sciences, said: “Obtaining the crystal structure of PARG is a first and key step to guide and illuminate future drug-design efforts aimed at treating certain cancers.

Knowing what this enzyme looks like, and having a good idea of how it operates, makes designing such drugs less of a shot in the dark.”

Dr Julie Sharp, senior science information manager at Cancer Research UK, added: “This discovery shows that bacteria and humans share similarities in the cellular machinery they use to repair damaged DNA. Importantly, knowing the structure of PARG in bacteria could help researchers design targeted treatments that are also effective in cancer patients.

We hope this will lead to further treatment options for patients with a range of cancers in the future.”