Scientists demonstrate potential new treatment for most common form of infant leukaemia

New drug could treat mixed-lineage leukaemia (MLL).

Cambridge scientists have shown that a potential new drug could treat mixed-lineage leukaemia (MLL), the most common form of leukaemia in babies, according to a study published in *Nature* yesterday (02 October).

MLL leukaemia is thought to account for up to 80 per cent of children below two years of age diagnosed with acute leukaemia, and up to one in 10 cases in adults.

Most patients don’t respond well to standard leukaemia treatments and often the cancer comes back.

The disease is caused when a gene called MLL gets fused to another gene.

This disrupts the normal function of MLL by creating a new ‘fusion protein’ that behaves inappropriately, switching on genes that drive the development of leukaemia.

The research team – based at the Wellcome Trust/Cancer Research UK Gurdon Institute and the Cambridge Institute for Medical Research at the University of Cambridge and with funding from the Cancer Research UK – collaborated with scientists from GlaxoSmithKline (GSK) and Cellzome AG to identify that the MLL-fusion proteins are targeted to leukaemia-causing genes by proteins from the BET family, which recognise certain chemical ‘tags’ on chromatin, the scaffold on which DNA is organised.

Together the researchers showed that a new chemical agent developed by GSK – I-BET151 – mimics these chemical tags, preventing BET and MLL from attaching to chromatin and activating the leukaemia genes.

Treatment of leukaemias in mice and human cancer cells in the lab showed that the chemical could halt the disease, paving the way for its use in patient trials.

Study co-leader Professor Tony Kouzarides, deputy director of the Wellcome Trust/Cancer Research UK Gurdon Institute at the University of Cambridge, said: “Our work shows that this type of leukaemia is reliant on MLL being able to bind to chromatin via BET proteins.

This “epigenetic” approach to therapy – which targets chromatin rather than DNA – is an exciting new avenue for drug discovery which we hope will be useful for other types of cancer in addition to MLL-leukaemias.”

Dr Brian Huntly, who co-led the study and is based at the Cambridge Institute for Medical Research at the University of Cambridge, said: “MLL leukaemia is very hard to treat and often the only option for patients who have become resistant to standard treatments is a bone marrow transplant.

We hope these findings may in future mean that fewer children need this procedure.”

Dr Lesley Walker, Cancer Research UK’s director of cancer information, said: “Cancer Research UK has played an important role in progress being made in childhood leukaemia, with eight in ten children now surviving more than five years compared to fewer than one in ten in the late 1960s.

But there is still more work to do and we urgently need better ways to treat children with more aggressive forms of leukaemia, such as MLL.

Although this research is only in the lab at the moment, we hope it will move quickly towards clinical trials in patients.”