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Scientists map out how childhood brain tumors relapse

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Researchers have discovered the unique genetic paths that the childhood brain tumour medulloblastoma follows when the disease comes back, according to research published in *Cancer Cell* today.

The study - funded by Cancer Research UK, Action Medical Research and others - shows that taking an extra tumour sample at recurrence, when there are no effective therapies, could identify subsets of patients that might be treatable with existing drugs that target the genetic faults.

The scientists, based at Newcastle University and The Institute of Cancer Research (ICR), looked at biopsies from the relapsed tumours of 29 patients. They found a range of changes that only appeared when the disease returned and were responsible for the cancer becoming more aggressive.

One particular combination of two genetic faults was common among a number of different subtypes, accounting for a very aggressive form of the disease.

The researchers then looked for ways to treat relapsed medulloblastomas in mice and were able to slow the growth of the tumour with an experimental drug that targets one of the faults.

Professor Steve Clifford, joint lead researcher based at Newcastle University, said: "Our study shows that we need to understand and treat relapsed medulloblastoma in a completely new way. It's clear that new

biopsies need to be taken when the disease returns to give doctors a clearer picture of the best and most appropriate treatment."

Around 60-70 per cent of children survive medulloblastoma, but for those patients who relapse the chance of survival is less than five per cent.

Dr Louis Chesler, Team Leader in Paediatric Solid Tumour Biology and Therapeutics at The Institute of Cancer Research, London, said: "We were very pleased to show in our study that some children with relapsed medulloblastoma could benefit from currently available targeted drugs, which usually have fewer and less severe side effects than traditional chemotherapy. It gives us a recipe to direct the use of targeted medicines in relapse where they are most needed.

"To personalise treatment to those who might benefit, doctors will need access to tumour samples as soon as children develop relapsed disease. Tumour biopsies are not routinely taken in these situations currently - and that will have to change before we can match the best treatments to the children who desperately need them."

Professor Peter Johnson, Cancer Research UK's chief clinician, said: "We urgently need new treatments that are effective in relapsed medulloblastoma - there are too few effective options that doctors can use. We're learning more all the time about how cancers evolve and change - in the short term this work will mean that doctors can decide on the most appropriate palliative care options for medulloblastoma but more importantly the research will lead to better treatments in the future."

More information: Hill, R.M. et al Combined MYC and TP53 defects emerge at medulloblastoma relapse and define rapidly progressive, therapeutically targetable disease, *Cancer Cell*, 2014.

Provided by Cancer Research UK