

PRESS RELEASE

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GENE EXPRESSION PATTERNS INDICATE WHICH OVARIAN CANCER PATIENTS WILL BENEFIT FROM TARGETED THERAPY

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Ovarian cancer is often detected at a late stage and is rarely curable. Many patients therefore receive the drug bevacizumab in addition to chemotherapy, as it blocks the tumour's blood supply – yet it does not help everyone, and it can sometimes cause serious side effects. A research team at the University Medical Centre Hamburg-Eppendorf, led by Prof. Dr. Barbara Schmalfeldt and Prof. Dr Leticia Oliveira-Ferrer in collaboration with bioinformatician Dr Olga Zolotareva (University of Kiel), has now succeeded in identifying a characteristic pattern of activity in the tumour that indicates who actually benefits from bevacizumab: patients with this pattern lived significantly longer when they received the drug. Surprisingly, the drug showed no discernible benefit in patients without this pattern. The Wilhelm Sander Foundation funded the project with 170,000 euros.

Ovarian cancer is one of the most dangerous forms of cancer affecting women. Fewer than half of those affected are still alive five years after diagnosis, despite very intensive treatment. The standard treatment consists of a complex operation followed by chemotherapy and adjuvant therapy. Doctors use the antibody bevacizumab for this: it inhibits the growth of blood vessels that supply the tumour and prolongs the period without disease progression. However, the drug does not work for all patients and can also cause side effects such as high blood pressure, kidney dysfunction or bleeding in the gastrointestinal tract. To date, there are no reliable criteria for predicting which patients will actually benefit from the treatment – so doctors must weigh up the options. Reliable tests to identify who will truly benefit are currently lacking.

Gene activity investigated in 244 tumour samples

To find out which patients actually benefit from antibody therapy, the team at the UKE's Department of Gynaecology examined tumour tissue from 212 patients who had been treated for advanced ovarian cancer between 2009 and 2017. The team analysed the gene activity of the tumour cells and specifically examined which genes were switched on or off. Complete treatment data were available for 181 women: 114 had received chemotherapy alone, whilst 67 had also received bevacizumab. Bioinformatician Dr Olga Zolotareva (University of Kiel) used computer programmes to search for groups of genes that are conspicuously active together in certain

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tumours. One challenge was that such patterns can easily arise by chance. The team therefore tested them on an independent group of 377 women from an earlier study, who had been examined using a different measurement technique. Only patterns that were detectable in both cohorts were taken into account.

Promising gene activity pattern identified

In fact, the researchers repeatedly identified activity patterns that could be reproduced independently in two further large cohorts of patients – in total, the team analysed data from over 1,000 patients. One pattern proved particularly significant: patients whose tumours exhibited over-activity of this gene pattern benefited considerably from bevacizumab – their risk of death fell by more than half compared with chemotherapy alone. In patients without this pattern, however, the drug showed no measurable survival benefit. What is remarkable is that this pattern had not previously been described and does not correspond to the known molecular subtypes of ovarian cancer.

Possible mechanism: stem cell-like tumour cells

The researchers suspect that the pattern is linked to the CTCFL gene. It helps cancer cells retain stem cell-like properties. Such cells grow faster and are more resilient. According to earlier studies, they may also be involved in the formation of new blood vessels themselves. In that case, a drug that specifically inhibits this angiogenesis could be particularly effective. This is, as yet, a hypothesis that requires further investigation.

The path to clinical application

The authors emphasise that the new biomarker is not yet ready for clinical use: ovarian cancer is so diverse that a single genetic pattern explains only part of the variation. Larger follow-up studies are needed, and ultimately a test that can be used in routine clinical practice. This is precisely where the team is focusing its efforts: it is already working on validating further datasets.

“What drives us are our patients, who urgently need more effective and targeted treatments,” says Prof. Dr Barbara Schmalfeldt. For this often fatal disease, the personalised use of bevacizumab would be an important step.

* The gender terms used in this text encompass all genders.

Wilhelm Sander-Stiftung: Forschung. Wissen. Zukunft.

The Wilhelm Sander Foundation has supported the research project with a total of around 170,000 euros. The foundation's purpose is to promote medical research, in particular projects aimed at combating cancer. Since the foundation was established,

a total of over 250 million euros has been disbursed to fund research in Germany and Switzerland. This makes the Wilhelm Sander Foundation one of the most significant private research foundations in the German-speaking world. It was established from the estate of the entrepreneur of the same name, who died in 1973.

University Medical Centre Hamburg-Eppendorf (UKE) – Department of Gynaecology

Founded in 1889, the University Medical Centre Hamburg-Eppendorf (UKE) is one of the most modern hospitals in Europe and, with around 17,000 staff, one of the largest employers in Hamburg. Each year, the UKE treats around 595,000 patients, 98,000 of whom are inpatients and 497,000 outpatients. The UKE's key research areas include, in particular, immunity, infections and inflammation, cardiovascular research, oncology, neurosciences and healthcare research. Around 3,500 students are studying medicine, dentistry and midwifery at the Faculty of Medicine, which is integrated into the UKE.

The UKE's Department of Gynaecology is one of the largest gynaecological departments in Germany and conducts research into cancers of the female reproductive organs, particularly ovarian and breast cancer. The team combines fundamental molecular research with clinical application to develop new diagnostic and therapeutic strategies. A key focus is on personalised medicine using molecular biomarkers.

For more information, visit: www.uke.de

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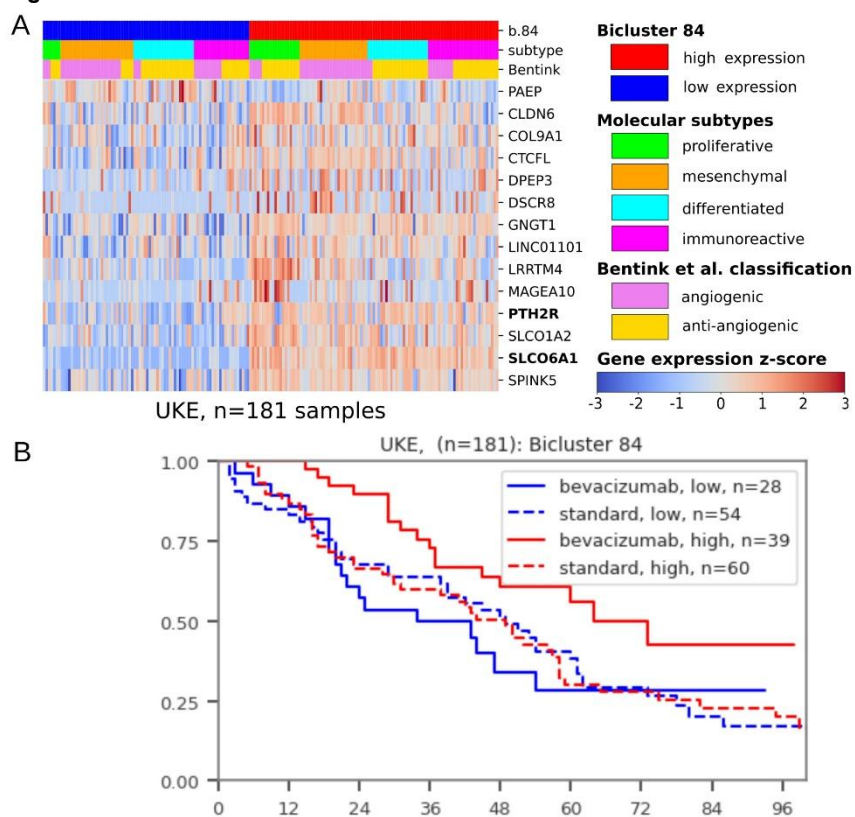
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Figure



Caption

Gene activity (Bicluster 84) divides ovarian tumours into two groups: where activity is high (red), patients benefit from bevacizumab; where it is low (blue), no benefit is apparent.

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