displays and sensors is an exciting prospect, but will be challenging to achieve. Unlike pigments, colours produced using this method are seen only in reflected light at certain viewing angles, and require lighting from a fixed direction, which might limit the range of possible applications. The extent to which the coloration effect can be used to manipulate and tailor the spectral signatures of reflected light remains unknown. However, this question can easily be explored, for example by incorporating pigments into the droplets to absorb specific wavelengths of light.

Another question is whether the full range of visible colours can be produced through systematic tuning of droplet shape and composition. This remains to be seen, but the range of colours achieved is already impressive, and the reported spectra are quite complex. It therefore seems possible that we could soon be able to fabricate surface structures that produce designed, iridescent patterns of light that are highly responsive to the environment and to the observer's location. ■

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MEDICAL RESEARCH

Sticking together helps cancer to spread

When cancer spreads, this metastatic stage of the disease is usually lethal. An analysis of immune cells that cluster with tumour cells in the bloodstream illuminates a partnership that might aid metastasis. SEE LETTER P.553

MIKALA EGEBLAD & KARIN E. DE VISSER

The process that determines whether cancer spreads from the original tumour site to reach distant organs is poorly understood, despite the devastating consequences for disease prognosis if this spreading step, termed metastasis, occurs. For cancer to invade other tissues and form metastases, tumour cells must travel through the body, including the bloodstream. Therefore, it can be an ominous sign if even low numbers of cancer cells, termed circulating tumour cells (CTCs), are found in blood samples[1]. If we can understand how CTCs survive in this environment, which is hostile partly because of forces (termed shear stress) encountered in blood vessels, this might enable the development of therapies to prevent metastasis. On page 553, Szczerba *et al.*[2] describe a previously unknown mechanism that enables CTCs to successfully colonize new sites in other tissues, and propose a possible vulnerability of CTCs that might offer a target for clinical treatments.

CTCs can associate with immune cells called white blood cells[3]. Szczerba *et al* studied blood samples from 70 people with an advanced stage of breast cancer and observed this type of association for an average of 3.4% of the CTCs in 34 of the patients. The authors investigated CTCs in five mouse models of breast cancer, and also found evidence that 0.05–61% of the CTCs in these models clustered with white blood cells. The authors report that the white blood cells mainly belonged to the most abundant immune-cell type in the blood, called neutrophils (Fig. 1).

Neutrophils have a crucial role in front-line defences against infectious agents. There is mounting evidence that these cells are key players in metastasis[4–8], but whether they have an effect on CTCs was unknown. Three observations led the authors to conclude that neutrophils clustering with CTCs can enhance the CTCs' metastatic potential. First, they found that the presence of CTC–neutrophil clusters in people with advanced breast cancer correlated with a shorter time until the disease advanced compared with the time until the disease advanced in people lacking these clusters. Second, when CTCs from CTC–neutrophil clusters were isolated from mice, separated from the neutrophils and injected into the bloodstream of tumour-free mice, they led to a considerably higher number of metastases than occurred in mice that received CTCs that had not been part of clusters with neutrophils. Third, if neutrophils were depleted in mice bearing breast tumours, this reduced the number of CTC–neutrophil clusters and delayed the formation of metastases in the lung compared with the situation in mice in which neutrophils were not depleted.

Why do neutrophil-associated CTCs metastasize more readily than CTCs that don't form this cellular partnership? To address this question, the authors characterized CTCs associated with neutrophils, and found that these cells had both a higher level of expression of

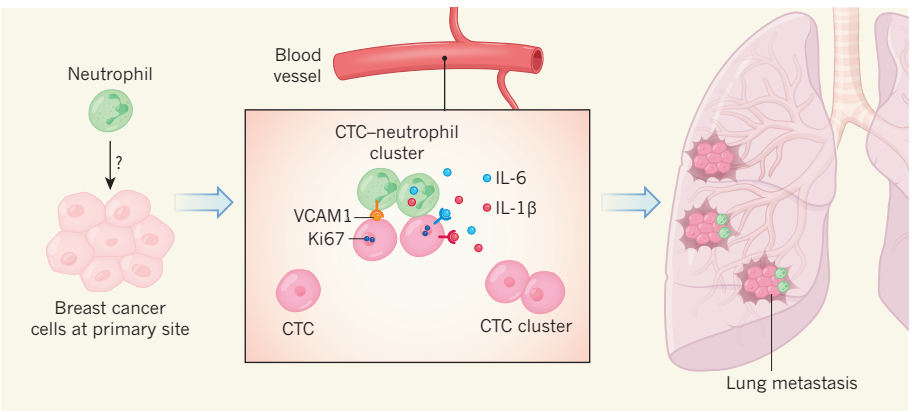

Figure 1 | Interactions between breast cancer cells and neutrophils promote the formation of lung metastases. When breast cancer cells spread from their primary site (a process termed metastasis), this is associated with poor prognosis. Szczerba *et al.*[2] report studies on clinical samples and mouse models which reveal that immune cells called neutrophils can boost the metastatic potential of tumour cells. It is not known whether neutrophils first interact with cancer cells in the primary tumour site in breast tissue. Metastatic breast cancer cells that have entered the bloodstream are called circulating tumour cells (CTCs), and they can exist individually or in clusters. The authors reveal that certain CTC clusters can also contain neutrophils. The protein VCAM1 on the tumour-cell surface is essential for the formation of these clusters, presumably because it binds to its corresponding receptor on neutrophils. Mutations in the gene *TLE1* (not shown) also promote the formation of CTC–neutrophil clusters, although the underlying mechanisms are unknown. Neutrophils clustered with CTCs express inflammatory signalling molecules, including the proteins IL-6 and IL-1β, and CTCs have the corresponding receptors for these proteins. Interactions between CTCs and neutrophils boost CTC cell-cycle progression, as indicated by the presence of a cell-cycle marker protein in the nucleus, called Ki67. The authors report that CTCs that have been associated with neutrophils are more likely to form metastases in the lung than are CTCs that have not. Whether the neutrophils remain associated with the cancer cells until they form such a metastasis is unknown.

genes associated with cell-cycle progression and a higher expression of the proliferation marker protein Ki67, compared with CTCs that were not associated with neutrophils. This cell-cycle-progression profile might indicate that neutrophil-associated CTCs are already primed to proliferate when they reach a secondary site.

The authors also identified pairs of inflammatory cytokine molecules and their corresponding receptors that defined CTC–neutrophil clusters. For example, CTC-associated neutrophils expressed the cytokines IL-1β and IL-6, and neutrophil-associated CTCs expressed the corresponding receptors for these cytokines. The authors found that *in vitro* exposure of mouse breast cancer cells to IL-1β and IL-6 increased their capacity to form lung metastases in mice. And when gene-editing was used to prevent the expression of the receptors for these cytokines in mouse cancer cells, expression of Ki67 was reduced in the neutrophil-associated CTCs. These findings suggest that communication between CTCs and neutrophils promotes the metastatic potential of the cancer cells.

A theme that has emerged in studies of the interactions between immune cells and cancer cells is the idea that the mutational profile of tumours can shape their crosstalk with immune cells[9]. Szczerba *et al*. indeed observed that patients with neutrophil-associated CTCs have a different spectrum of mutations in their cancer cells from that found in the cancer cells of patients without neutrophil-associated CTCs. One of the frequently observed mutations in tumour cells of people with breast cancer who had CTC–neutrophil clusters was in the *TLE1* gene, and the presence of this mutation in mouse cancer cells was shown to enhance cluster formation between CTCs and neutrophils. How mutations in *TLE1* affect clustering is unknown. The authors also discovered that the cell-adhesion protein VCAM1 is essential for clustering between CTCs and neutrophils in mice.

Several mechanisms have been reported[5,7,10] by which neutrophils can promote metastasis, including by protecting cancer cells against attack by immune cells, or supporting cancer cells in their invasion of another tissue. Szczerba and colleagues add a new mechanism to the list: the possibility that neutrophils support cancer cells in their journey through the bloodstream to secondary sites.

The authors' results suggest that interrupting the formation of CTC–neutrophil clusters might offer a strategy for preventing metastasis, and that the mutational profile of the primary tumour, such as the presence of *TLE1* mutations, could indicate which patients are likely to develop CTC–neutrophil clusters and thus might benefit from cluster-disrupting therapeutic interventions.

Looking ahead, several key issues should be addressed before attempts are made to target CTC–neutrophil clustering in the clinic. Most crucially, it remains to be determined whether neutrophils cause the increased metastatic potential of CTCs, or instead tend to cluster with CTCs that have a high metastatic potential. Although neutrophil depletion inhibited the formation of lung metastases in Szczerba and colleagues' study, this approach not only blocks CTC–neutrophil clustering, but also prevents other pro-metastatic functions of neutrophils. One way of specifically investigating the connection between neutrophil–CTC clustering and metastasis could be to trace the fate of CTCs that have been genetically engineered to lack VCAM1, thus interfering with their ability to associate with neutrophils. Would such CTCs be able to make it from their primary site to a secondary site, and, if they could, would they be unable to proliferate or be eliminated by immune cells?

Another central issue is to define the window of therapeutic opportunity for interventions that target CTC clustering with neutrophils. It is not known whether neutrophils and cancer cells cluster in the primary tumour and then enter the bloodstream together. Also unknown is whether detection of CTC–neutrophil clusters in the blood signifies that other neutrophil-associated CTCs have already established metastases. A suitable system in which to address these matters would be genetically engineered mouse models of cancer that recapitulate the stepwise progression of cancer in tandem with coevolving immune-cell responses. Such animals would provide a more faithful model of the course of progression of human cancer than the mouse models used by Szczerba and colleagues, which were mainly immunodeficient.

Szczerba *et al*. have provided important insights that are relevant to the growing body of work indicating how neutrophils promote metastasis and how CTCs interact with other types of blood cell. As we learn more about the cellular interactions that affect metastasis, we could be moving closer to generating much-needed treatments to stop cancer in its tracks. ■

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QUANTUM PHYSICS

New ways to encode and use quantum bits

Quantum computers require controlled encoding to protect computations from environmental noise. Two experiments have achieved such encoding using what are known as infinite-dimensional quantum systems. SEE LETTERS P.509 & P.513

ALESSANDRO FERRARO

Transmitting or manipulating information in a noisy environment typically requires some form of encoding and error correction. If these precautions are necessary when information is carried by classical physical systems, they are even more so when the carriers are fragile quantum systems. However, quantum encoding is notoriously difficult, because the laws of quantum mechanics impose severe constraints — for example, a single quantum object cannot be copied, which hinders simple encoding schemes. Consequently, the manipulation of encoded quantum systems, which is necessary for error correction, can be extremely involved. On pages 513 and 509, Flühmann *et al.*[1] and Gao *et al.*[2] report promising methods for encoding and manipulating quantum information using, respectively, the state of motion of a trapped ion and the state of multiple photons in superconducting cavities.

Quantum systems can be classified into two categories, depending on the dimensionality of the parameter space that is needed to describe their features accurately. On the one hand, there are quantum features that require a finite dimension. An example is the magnetic moment of an electron, which has only two distinguishable states and is therefore represented in a 2D space. Such features