Mechanisms of cardiovascular disease and cancer give clues to new therapies

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Cardiovascular conditions leading to heart attacks and strokes are treated quite separately from common cancers of the prostate, breast or lung, but now turn out to involve some of the same critical mechanisms at the molecular level. This in turn provides clues to more effective therapies for both cancer and cardiovascular diseases, but requires researchers in these distinct fields to come together. The seeds were sown for closer cooperation between these two groups at a recent workshop organised by the European Science Foundation (ESF), which also highlighted the striking progress already made in understanding key common mechanisms underlying both disease categories.

The workshop kicked off by considering one of the most important molecular processes common to a number of cancers and cardiovascular disease, involving the pathway known as the endothelin axis. The endothelium is the thin layer of cells lining every blood vessel of the body from the smallest capillaries to the largest arteries and even the heart itself.

This layer separates the blood from the vessel walls and the smooth muscles whose contractions restrict and control blood flow. These muscle contractions are controlled by proteins called endothelins manufactured by the endothelium cells, and if there are too many of them blood flow is restricted too much, leading to hypertension (high blood pressure) and participating in other conditions such as acute coronary syndrome and stroke. However some endothelins are also signalling molecules promoting growth and retarding the natural process

of apoptosis (cell death) involved in eliminating cells.

Some tumour cells, for example in ovarian carcinoma, exploit endothelins to suppress their death while migrating to other parts of the body in the metastasis process, enabling the tumour to spread, usually with fatal results.

Understanding the endothelin axis and its role in both cancer and cardiovascular disease is now increasing as a result of collaboration between these two medical research fields spawned by the ESF workshop and similar events elsewhere in the world. But until recently the role of endothelins had been studied mostly in the context of cardiovascular disease rather than cancer, according to M. Giovanna Trivella, the ESF workshop's convenor from the Institute of Clinical Physiology at the National Research Council of Italy (CNR) in Pisa.

Conversely, angiogenesis, which is the sprouting of new blood vessels from existing ones, has been studied mostly for its role in tumour growth, and not so much as a possible therapy for heart disease by developing new blood vessels to replace existing damaged ones. Yet the same underlying molecular pathways are at work in both cases, with great potential for synergy between the two research camps.

The workshop also heard how the overlap between cancer and cardiovascular disease was not of concern purely for research and development of new therapies, but also had practical considerations for immediate treatment now. "Many patients who receive chemotherapies develop heart failure symptoms, and the cardiologists have to interact with the oncology (cancer) specialists to make complex therapeutic decisions," said Trivella. So there is already interaction between the two groups out in the hospitals.

There has also been an overlap for some years in the imaging

technologies that play a role in studying both types of disease in the laboratory. Positron electron tomography in particular has been used in both fields, producing images of the body region, such as a tumour, under study. "The Positron Electron Tomography Laboratory started years ago has been used to study the field of cardiac microcirculation and ischemic myocardial metabolism, and yet later on it also became a powerful tool in oncological diagnostic procedures," said Trivella.

There is also overlap between cardiovascular disease and cancer at the level of gene expression and regulation within cells, and in particular the role of small RNA molecules called micro RNAs. These molecules do not perform the role of RNA as traditionally understood in carrying genetic information from the DNA of genes to the protein factories called ribosomes. Instead they control the expression of genes themselves, and when this goes wrong, inflammatory processes can be triggered that in turn increase the risk of both cardiovascular diseases and cancers. "The future direction is to investigate whether and how the different gene networks regulated by micro RNAs are organized as a whole," said Giuseppe Rainaldi, the co-convenor of the workshop. "These studies will be necessary in order to understand complex biological processes and to approach micro RNA based therapy in a more efficient way."

Source: European Science Foundation