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1 **Preface: Extracellular vesicles in the tumour microenvironment**

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16
17 Cancer is a devastating disease that touches the lives of millions of people around the world. After
18 many years of work by thousands of scientists and clinicians around the globe the overall survival of
19 patients who acquire certain types of cancer has been dramatically improved. However, the overall
20 survival rates for some forms of cancer remain stubbornly low. It is therefore imperative to devise
21 novel avenues of research from which to derive new opportunities for drug development and
22 identification of new tools for early diagnosis and disease monitoring.

23
24 One such emerging area of intensive research is the concept of the tumour microenvironment.
25 Cancer cells do not grow as a homogenous mass, existing in isolation from other cell types, but
26 rather in collaboration with other cells in the environment of the tumour. These stromal cells, which
27 under normal conditions support the function of healthy tissues, surround and perfuse the tumour
28 mass and interact with cancer cells. This communication in the tumour microenvironment often
29 leads to the corruption of the stromal cells, allowing them to inappropriately stimulate and support
30 the growth of the tumour. Understanding the signalling mechanisms between the different cells of
31 the tumour microenvironment holds promise as the key to developing new therapeutics that could
32 block the cancer's support mechanism.

33
34 Extracellular vesicles (EVs) are small lipid-bound vesicles released by cells into the extracellular
35 space. Initially thought of as a biological curiosity, they are now known to be important messengers
36 mediating the dialogue between cells. The cargo they carry can either be internalised and utilised by
37 recipient cells or interact with receptors at the plasma membrane leading to intracellular signalling.
38 One cell can therefore affect the phenotype of another cell via the transfer of EVs with specific types
39 of cargo such as RNA or protein. EVs have been shown to have a number of roles, including in
40 regulating the immune system, angiogenesis and stress responses. Importantly, their dysregulation
41 can have pathological effects and their abnormal function has been implicated in cancer.

42
43 The combination of these two novel fields has led researchers to study the role of EVs in the tumour
44 microenvironment. This convergence of disciplines has led to exciting new insight into the way in
45 which tumours are affected by EV-mediated communication between cancer and stromal cells. Like
46 any new field with promise it needs to be nurtured and supported. For this reason the Royal Society
47 held a Science Meeting in January 2017 entitled "Extracellular Vesicles and the Tumour
48 Microenvironment". This exciting meeting was well attended and led to this special edition of the

49 Philosophical Transactions B. In this special edition we start with a more detailed introduction to the
50 topic and the meeting. The rest of the special edition, which includes reviews, opinion pieces and
51 research articles, describes various aspects of EV biology in the tumour microenvironment. The
52 review articles and opinion pieces cover a range of aspects, including EV heterogeneity, the role of
53 lipids and EVs in tumour progression, EVs in cell senescence, cell death and immune function, and
54 the way in which miRNAs carried by EVs can act as ligands to trigger the activation of receptor
55 proteins. The research articles describe how EVs released by ovarian cancer cells treated with
56 chemotherapy can affect other cells in the vicinity leading to tumour progression, and how EVs
57 released by glioblastoma cells can alter human astrocytes leading them to be pro-tumorigenic.

58

59 The exciting field of EVs in the tumour microenvironment is growing rapidly. Greater understanding
60 could lead to novel therapeutics to tackle cancer, and new tools to aid diagnosis and prognosis. We
61 hope that readers will enjoy this special edition of Philosophical Transactions B, which sheds light on
62 this expanding field.

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