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Contact: Anne-Marie Clarke

anne-marie.clarke@qub.ac.uk

44-028-909-75320

Queen's University Belfast

Cancer breakthrough to prevent heart failure and increase survival rates

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Scientists at Queen's Centre for Vision and Vascular Science have discovered the role of an enzyme which, when a patient receives chemotherapy, can cause life-threatening damage to the heart. This has, until now, restricted the amount of chemotherapy doses a patient can receive; but while protecting the heart, this dilutes the chemotherapy's effectiveness in destroying cancerous tumours.

By identifying the role of the enzyme - NADPH oxidase - work can now go ahead into making chemotherapy treatments more effective and reduce the toxic effects of cancer treatment on the heart.

Dr David Grieve, jointly leading on the research at Queen's School of Medicine, Dentistry and Biomedical Sciences said: "While chemotherapy drugs are highly effective in treating a wide range of tumours, they can also cause irreversible damage to the heart. This means that doctors are restricted in the doses they can administer to patients. In recent years, scientists have been searching for new drugs to prevent these side-effects.

"Although we have known about the NADPH oxidase enzyme for many years, until now, we were not aware of its crucial role in causing heart damage associated with chemotherapy. Our research findings

hold clear potential for the creation of new drugs to block the action of the enzyme, which could significantly reduce heart damage in cancer patients.

"Ultimately, this could allow for the safer use of higher doses of chemotherapy drugs and make the treatment more effective against tumours. Despite improved treatments, cancer is currently responsible for 25 per cent of all mortality in the western world. By reducing the risk of heart failure associated with chemotherapy, patient survival rates could be significantly increased."

Scientists at Queen's are now concentrating their efforts on further studies to define the precise role of NADPH oxidase in the development of heart failure associated with cancer therapies. It is hoped that these may lead to the development of a drug which would have the potential to save lives among cancer patients.

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The research by Dr David Grieve and Professor Barbara McDermott was funded by the British Heart Foundation in Northern Ireland and published in leading international journal, *Cancer Research*.

Media inquiries to Anne-Marie Clarke at Queen's University Communications Office on 00 44 (0)28 9097 5320 or email anne-marie.clarke@qub.ac.uk

Notes to Editors

1. Dr David Grieve is available for interview. Interview bids and photo requests to Anne-Marie Clarke on 00 44 (0)28 9097 5320 or email anne-marie.clarke@qub.ac.uk

2. This research was published in the leading international journal, *Cancer Research* (Volume 70 (22); pages 9287).

3. Enzymes are proteins that catalyse (increase or decrease the rates of) chemical reactions.

4. Around 7 per cent of cancer patients treated with the upper limit dosage of chemotherapy agent Doxorubicin currently develop heart failure. Doxorubicin is commonly used in the treatment of a wide range of cancers. Its most serious adverse effect is life-threatening heart damage. The drug is administered intravenously, in the form of hydrochloride salt. The drug was originally isolated in the 1950s from bacteria found in soil samples taken from Castel del Monte, an Italian castle.

5. The Centre for Vision & Vascular Science is one of the four Research Centres within the newly reconfigured School of Medicine, Dentistry and Biomedical Sciences. The Centre's research is multidisciplinary in nature, with an integrated mixture of approaches ranging from basic cell and molecular biology, pathophysiology of disease, genetic analysis, protein chemistry, patient-based investigation and clinical trials (www.qub.ac.uk/cvvs)

6. Dr David Grieve: After being awarded an honours degree at University of Dundee in 1995, David moved to The Royal Veterinary College in London where he completed his PhD thesis on "The role of dietary lipoproteins in the initiation of atherosclerosis" in 1998. He was then appointed as a post-doctoral scientist by Professor Ajay Shah in the newly established Cardiovascular Division at King's College London, where he worked for almost 7 years and received comprehensive training in cardiovascular research. In 2005, he became a Lecturer in Cardiovascular Physiology within the School of Medicine, Dentistry and Biomedical Sciences at Queen's University Belfast where he has now established his own research group. He has secured over £1 million in competitive grant funding, £800,000 of which has been as Principal Investigator. He has published over 30 peer-reviewed papers in the top journals in his subject area, including Circulation, Circulation Research, Journal of the American College of Cardiology and European Heart Journal. These publications carry an average impact factor of 6.5 and have received over 1200 citations. He has published over 60 peer-reviewed conference abstracts which have been largely presented at the main cardiovascular research meetings such as the American Heart Association and International Society for Heart Research (ISHR). His main research interest is focussed on the mechanisms underlying the development and progression of cardiovascular remodeling and dysfunction, with a particular interest in oxidative stress, diabetes, and the novel actions of incretin peptide hormones.
