

(Contact, photo of the group, affiliation, country, brief description to their interest in NO and related projects, major publications, and link to their lab website)

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Interest in NO and Cancer:

The central theme of my laboratory is to explore how inflammation derived from nitrosative stress and human endogenous retrovirus activation influences tumour biology, modifies the tumour microenvironment and influences treatment responses and patient outcomes. A major source of nitric oxide (NO) and nitrosative stress in tumours comes from inducible nitric oxide synthase (iNOS), and correlates with increased risk of poor outcomes and distant metastasis. Our research is exploring the pro- and anti-tumour effects of NO in cancer biology including cellular response to stressors such as DNA damage, oncogene activation, altered cell metabolism and deregulating DNA repair enzymes and tumour suppressor genes, in addition to modulation of apoptotic and metastatic processes.

Our research also explores the role of HERV-K in tumour biology. HERV-K has been found to be activated in many tumour types including breast and prostate cancer, and is associated with increased risk of poor outcomes. Using in vitro models of breast and prostate cancer, we are examining the role of HERV-K derived proteins (Gag, Env, Rec and Np9) on tumour cell phenotype and signal transduction pathways. Coupled with our patient cohort studies this allows us to then validate our findings for clinical importance.

Finally we also seek to understand the impact of these tumour epithelium expressed inflammatory mediators on the larger tumour microenvironment using 3D spheroid co-culture models and via multiplex protein and RNA imaging of tumours with our US based collaborators at the National Cancer Institute and Houston Methodist Hospital. Sharon has been awarded a number of grants including a SFI Career Development Award, Breast Cancer Now Project and PhD Grants, and Irish Cancer Society Funding and is a CÚRAM SFI Research Centre for Medical Devices funded investigator.

Selected Major Publications:

1. Khan FH, Dervan E, Bhattacharyya DD, McAuliffe JD, Miranda KM, Glynn SA. The Role of Nitric Oxide in Cancer: Master Regulator or NOt? *Int J Mol Sci.* 2020 Dec 10;21(24):9393. doi: 10.3390/ijms21249393.
2. Alsharabasy AM, Glynn SA, Pandit A. The role of extracellular matrix in tumour angiogenesis: the throne has NOx servants. *Biochem Soc Trans.* 2020 Dec 18;48(6):2539-2555. doi: 10.1042/BST20200208.
3. Walsh EM, Shalaby A, O'Loughlin M, Keane N, Webber MJ, Kerin MJ, Keane MM, Glynn SA, Callagy GM. Outcome for triple negative breast cancer in a retrospective cohort with an emphasis on response to platinum-based neoadjuvant therapy. *Breast Cancer Res Treat.* 2019 Feb;174(1):1-13. doi: 10.1007/s10549-018-5066-6.
4. Glynn SA. Emerging Novel Mechanisms of Action for Nitric Oxide in Cancer Progression. *Current Opinions in Physiology.* *Current Opinion in Physiology.* 2019 Jun 1; 9:18-25. doi: 10.1016/j.cophys.2019.03.010
5. Ridge SM, Bhattacharyya D, Dervan E, Naicker SD, Burke AJ, Murphy JM, O'leary K, Greene J, Ryan AE, Sullivan FJ, Glynn SA. Secreted factors from metastatic prostate cancer cells stimulate mesenchymal stem cell transition to a pro-tumourigenic 'activated' state that enhances prostate cancer cell migration. *Int J Cancer.* 2018 May 15;142(10):2056-2067. doi: 10.1002/ijc.31226.
6. Basudhar D*, Glynn SA*, Greer M, Somasundaram V, No JH, Scheiblin D, Garrido P, Heinz W, Ryan AE, Wiess J et al. Co-expression of NOS2 and COX2 accelerates tumor growth and reduces survival in estrogen receptor-negative breast cancer. *Proc Natl Acad Sci U S A.* 2017 Dec 5;114(49):13030-13035. doi: 10.1073/pnas.1709119114.
7. Garrido P, Shalaby A, Walsh EM, Keane N, Webber M, Keane MM, Sullivan FJ, Kerin MJ, Callagy G, et al, & Glynn SA. Impact of inducible nitric oxide synthase (iNOS) expression on triple negative breast cancer outcome and activation of EGFR and ERK signaling pathways. *Oncotarget.* 2017 Jul 26;8(46):80568-80588. doi: 10.18632/oncotarget.19631.
8. Burke AJ, Garrido P, Johnson C, Sullivan FJ, Glynn SA. Inflammation and Nitrosative Stress Effects in Ovarian and Prostate Pathology and Carcinogenesis. *Antioxid Redox Signal.* 2017 Jun 20;26(18):1078-1090
9. Ridge S, Sullivan FJ, Glynn SA. Mesenchymal Stem Cells: Key Players in Cancer Progression. *Molecular Cancer.* *Mol Cancer.* 2017 Feb 1;16(1):31.
10. Burke AJ, Ali H, O'Connell E, Sullivan FJ, Glynn SA. Sensitivity Profiles of Human Prostate Cancer Cell Lines to an 80 Kinase Inhibitor Panel. *Anticancer Res.* 2016 Feb;36(2):633-41.
11. Prueitt R*, Wallace TA*, Glynn SA*, Yi M, Tang W, Luo J, Dorsey TH, Stagliano KE, Gillespie JW, Hudson RS, Terunuma A, Shoe JL, Haines DC, Yfantis HG, Han M, Martin DN, Jordan SV, Borin JF, Naslund MJ, Alexander RB, Stephens RM, Loffredo CA, Lee DH, Putluri N, Sreekumar A, Hurwitz AA, Ambs S. An immune-inflammation gene expression signature in prostate tumors of smokers. *Cancer Res.* 2016 Mar 1;76(5):1055-65.
12. Walsh EM, Keane MM, Wink DA, Callagy G, Glynn SA. Review of Triple Negative Breast Cancer and the Impact of Inducible Nitric Oxide Synthase on Tumor Biology and Patient Outcomes. *Crit Rev Oncog.* 2016;21(5-6):333-351. doi: 10.1615/CritRevOncog.2017021307.
13. Wallace TA, Downey R, Seufert CJ, Schetter A, Dorsey TM, Goldman R, Yan P, Sullivan FJ, Giles FJ, Wang-Johanning F, Ambs S, Glynn SA. Elevated HERV-K mRNA expression in PBMC is

- associated with a prostate cancer diagnosis particularly in older men and smokers. *Carcinogenesis* 2014 May 23. pii: bgu114. IF = 5.2.
14. Heinecke JL, Ridnour LA, Cheng RY, Switzer CH, Lizardo MM, Khanna C, Glynn SA, Hussain SP, Young HA, Ambs S, Wink DA. Tumor microenvironment-based feed-forward regulation of NOS2 in breast cancer progression. *Proc Natl Acad Sci U S A*. 2014 Apr 29;111(17):6323-8.
 15. Burke AJ, Giles FJ, Sullivan, FJ, Glynn SA. The Yin and Yang of nitric oxide in cancer progression. *Carcinogenesis*. 2013 Mar;34(3):503-12. IF = 5.2
 16. Switzer CH, Cheng RY, Ridnour LA, Glynn SA, Ambs S, Wink DA. Ets-1 is a transcriptional mediator of oncogenic nitric oxide signaling in estrogen receptor-negative breast cancer. *Breast Cancer Res*. 2012 Sep 12;14(5):R125. IF = 5.9
 17. Ridnour LA, Barasch KM, Windhausen AN, Dorsey TH, Lizardo MM, Yfantis HG, Lee DH, Switzer CH, Cheng RY, Heinecke JL, Brueggemann E, Hines HB, Khanna C, Glynn SA, Ambs S, Wink DA. Nitric Oxide Synthase and Breast Cancer: Role of TIMP-1 in NO-mediated Akt Activation. *PLoS One*. 2012;7(9):e44081. doi: 10.1371/journal.pone.0044081. IF = 3.5
 18. Switzer CH, Glynn SA, Cheng RY, Ridnour LA, Green JE, Ambs S, Wink DA. S-Nitrosylation of EGFR and Src Activates an Oncogenic Signaling Network in Human Basal-Like Breast Cancer. *Mol Cancer Res*. 2012 Sep;10(9):1203-15. IF = 4.5
 19. Wang-Johanning F, Rycaj K, Plummer JB, Li M, Yin B, Frerich K, Garza JG, Shen J, Lin K, Yan P, Glynn SA, Dorsey TH, Hunt KK, Ambs S, Johanning GL. Immunotherapeutic potential of anti-human endogenous retrovirus-K envelope protein antibodies in targeting breast tumors. *J Natl Cancer Inst*. 2012 Feb 8;104(3):189-210. IF = 15.2
 20. Ambs S, Glynn SA. Candidate pathways linking inducible nitric oxide synthase to a basal-like transcription pattern and tumor progression in human breast cancer. *Cell Cycle*, 2011 Feb 15;10(4):619-24. IF 5.0
 21. Glynn SA, Prueitt RL, Ridnour LA, Boersma BJ, Dorsey TM, Wink DA, Goodman JE, Yfantis HG, Lee DH, Ambs S. COX-2 activation is associated with Akt phosphorylation and poor survival in ER-negative, HER2-positive breast cancer. *BMC Cancer*. 2010 Nov 15;10:626. doi: 10.1186/1471-2407-10-626. IF = 3.3
 22. Glynn SA, Boersma BJ, Martin D, Howe TM, Ridnour LA, Wink DA, Yi M, Stephens RM, Yfantis HG and Ambs S. NOS2 predicts survival in estrogen receptor-negative breast cancer and is associated with a prognostic basal-like transcription pattern. *J Clin Invest*. 2010 Nov;120(11):3843-54. doi: 10.1172/JCI42059. IF = 13.8
 23. Glynn SA, Boersma BJ, Howe TM, Edvardsen H, Geisler S, Goodman JE, Ridnour LA, Lonning PE, Børresen-Dale AL, Naume B, Kristensen VN, Chanock SJ, Wink DA, and Ambs S (2009) A mitochondrial targeting sequence polymorphism in the MnSOD gene predicts inferior survival in breast cancer patients treated with cyclophosphamide. *Clinical Cancer Research*, 15(12) 4165-73. doi: 10.1158/1078-0432.CCR-09-0119. IF= 8.2
 24. Glynn SA, O'Sullivan D, Eustace AJ, Clynes M, O'Donovan N. The 3-hydroxy-3-methylglutaryl-coenzyme A reductase inhibitors, simvastatin, lovastatin and mevastatin inhibit proliferation and invasion of melanoma cells. *BMC Cancer*. 2008 Jan 16;8(1):9. doi: 10.1186/1471-2407-8-9. IF=3.3
 25. Glynn SA, Gammell P, Heenan M, O'Connor R, Liang Y, Keenan J and Clynes M. (2004) A new superinvasive in vitro phenotype induced by selection of human breast carcinoma cells with the chemotherapeutic drugs paclitaxel and doxorubicin. *Br J Cancer*, 91, 1800-1807. IF = 4.8