Title: Evaluation of the ability of an oxygen carrier to increase radiosensitivity in a BxPC3 model under normoxic/hypoxic conditions

Author & institute:

Xuehua Lin[1], Maitiú Ó Murchú[1, 2], Ian Miller[3], Brenton Cavanagh[4], Abhik Mallick[5], David Hackett[2], Jacintha O'Sullivan[2], Stephen G. Maher[2], Helena Kelly[1]

[1]School of Pharmacy and Biomolecular Sciences, RCSI University of Medicine and Health Sciences, Dublin, Ireland.
[2]Trinity St. James's Cancer Institute, Department of Surgery, St. James's Hospital and Trinity College Dublin, Dublin, Ireland.
[3] Dept. of Physiology and Medical Physics, RCSI University of Medicine and Health Sciences, Dublin, Ireland
[4]RCSI Cellular and Molecular Imaging Core, RCSI University of Medicine and Health Sciences, Dublin, Ireland

[5]School of Medicine, National University of Ireland Galway, Galway, Ireland

Abstract body:

Radiation (RT) has long been a powerful weapon against solid tumours. Oxygen is recognized as a potent chemical radiosensitizer that enhances radiation efficacy. However, hypoxia is a common feature of solid tumours, which is a major contributor to radiation resistance. Known for being extremely hypoxic, pancreatic ductal adenocarcinoma (PDAC) poorly responds to radiation. Methods to increase oxygen levels in PDAC are therefore desirable. Perfluorocarbons (PFCs) capable of loading significant amount of oxygen have emerged as a promising oxygen carrier. Therefore we formulated a PFC nanoemulsions (NeVP), which showed stability upto 6 months with a droplet size of ~150 nm, a PDI of < 0.3. NeVP with the ability of loading oxygen upto 600 mmHg had oxygen release for upto 12 hours in an open environment. In a BxPC-3 model and under normoxic conditions, treatment with NeVP blank (NeVP) and loaded with oxygen (oxyNeVP) in combination with 4Gy radiation both increased sensitivity to ionizing radiation with a clonogenic assay showing significantly decreased BxPC-3 colony formation. In addition, γ-H2AX-probed western blot showed these treatments also stopped radiation-induced DNA damage from being repaired in normoxic conditions. In hypoxic conditions both NeVP and OxyNeVP reversed the effects of hypoxia with HIF-1α significantly degraded in BxPC-3 cells. However only oxyNeVP increased sensitivity to radiation (4 Gy) causing a significant reduction in colony formation in a clonogenic assay. In conclusion, our oxygenated nanoemulsions is a promising system to alleviate hypoxia and effectively enhance radiation response.