Christopher Lord, Ph.D.

Current Position:	Senior Staff Scientist The Breakthrough Breast Cancer Research Centre The Institute of Cancer Research
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EDUCATION

1997	DPhil	University of Oxford, UK
1993	BSc (Hons)	University of Surrey, UK

PREVIOUS POSTS HELD

Aug 2005-Sep 2008	Staff Scientist	Institute of Cancer Research, UK
Oct 2000-Aug 2005	Postdoctoral Fellow	Institute of Cancer Research, UK
Jul 1997-Oct 2000	Postdoctoral Fellow	Cambridge Institute for Medical Research, University of Cambridge, UK

BIOGRAPHY

Chris Lord received his PhD in 1997 (University of Oxford), working in the field of complex trait genetics. Since 2000, Chris has worked at the Breakthrough Breast Cancer Research Centre at the Institute of Cancer Research, London. Here Chris' work has focussed upon the use of genetics to identify novel therapeutic approaches to cancer as well as using high-throughput genetic screens to optimise the use of existing cancer drugs. In 2005, Chris was a member of the team that demonstrated the potential of PARP inhibitors in BRCA mutant cancers and his subsequent work has also shown that PARP inhibitors could be used in patients with tumours that carry PTEN defects.

CURRENT PROJECTS

Refining the clinical use of PARP inhibitors in cancer; development of biomarkers for use with PARP inhibitors; oncogenomics; DNA repair; drug resistance; drug development

CAREER HIGHLIGHTS

- Identifying BRCA dysfunction as a determinant of PARP inhibitor sensitivity (Nature 2005).
- Identification of additional determinants of PARP inhibitor sensitivity (publications in 2005, 2006, 2008).
- Identifying a genetic mechanism of resistance to PARP inhibitors (Nature 2008).
- Identifying novel determinants of tamoxifen sensitivity (Cancer Cell 2008)
- Identifying novel synthetic lethal strategies for MMR deficient cancers (Cancer Cell 2010)

PUBLICATIONS
60 publications in peer-reviewed journal

Publications selected for PARP and BRCA (* corresponding or joint first author)

1. Sourisseau T, Maniotis D, McCarthy A, Tang C, Lord CJ, Ashworth A, Linardopoulos S.: Aurora-A expressing tumour cells are deficient for homology-directed DNA double strand-break repair and sensitive to PARP inhibition. EMBO Mol Med. 2010 Apr;2(4):130-42.
2. Mendes-Pereira AM, Martin SA, Brough R, McCarthy A, Taylor JR, Kim JS, Waldman T, Lord CJ, Ashworth A.: *Synthetic lethal targeting of PTEN mutant cells with PARP inhibitors. EMBO Mol Med. 2009 Sep;1(6-7):315-22.
3. Martin SA, Hewish M, Lord CJ, Ashworth A.: *Genomic instability and the selection of treatments for cancer. J Pathol. 2010 Jan;220(2):281-9.
4. Oliver AW, Swift S, Lord CJ, Ashworth A, Pearl LH.: Structural basis for recruitment of BRCA2 by PALB2. EMBO Rep. 2009 Sep;10(9):990-6
5. McCabe N, Cerone MA, Ohishi T, Seimiya H, Lord CJ, Ashworth A.: *Targeting Tankyrase 1 as a therapeutic strategy for BRCA-associated cancer. Oncogene. 2009 Mar 19;28(11):1465-70.
6. Lord CJ, McDonald S, Swift S, Turner NC, Ashworth A.: *A high-throughput RNA interference screen for DNA repair determinants of PARP inhibitor sensitivity. DNA Repair (Amst). 2008 Dec 1;7(12):2010-9.
7. Lord CJ, Ashworth A.: *Targeted therapy for cancer using PARP inhibitors. Curr Opin Pharmacol. 2008 Aug;8(4):363-9
8. Turner NC, Lord CJ, Iorns E, Brough R, Swift S, Elliott R, Rayter S, Tutt AN, Ashworth A.: A synthetic lethal siRNA screen identifying genes mediating sensitivity to a PARP inhibitor. EMBO J. 2008 May 7;27(9):1368-77.
9. Martin SA, Lord CJ, Ashworth A.: *DNA repair deficiency as a therapeutic target in cancer. Curr Opin Genet Dev. 2008 Feb;18(1):80-6.
10. Edwards SL, Brough R, Lord CJ, Natrajan R, Vatcheva R, Levine DA, Boyd J, Reis-Filho JS, Ashworth A.: Resistance to therapy caused by intragenic deletion in BRCA2. Nature. 2008 Feb 28;451(7182):1111-5
11. Brough R, Wei D, Leulier S, Lord CJ, Rong YS, Ashworth A.: Functional analysis of Drosophila melanogaster BRCA2 in DNA repair. DNA Repair (Amst). 2008 Jan 1;7(1):10-9.
12. Gudmundsdottir K, Lord CJ, Ashworth A.: The proteasome is involved in determining differential utilization of double-strand break repair pathways. Oncogene. 2007 Nov 29;26(54):7601-6.
13. Lord CJ, Ashworth A.: RAD51, BRCA2 and DNA repair: a partial resolution. Nat Struct Mol Biol. 2007 Jun;14(6):461-2.
14. Tutt AN, Lord CJ, McCabe N, Farmer H, Turner N, Martin NM, Jackson SP, Smith GC, Ashworth A.: Exploiting the DNA repair defect in BRCA mutant cells in the design of new therapeutic strategies for cancer. Cold Spring Harb Symp Quant Biol. 2005;70:139-48.
15. McCabe N, Lord CJ, Tutt AN, Martin NM, Smith GC, Ashworth A.: BRCA2-deficient CAPAN-1 cells are extremely sensitive to the inhibition of Poly (ADP-Ribose) polymerase: an issue of potency. Cancer Biol Ther. 2005 Sep;4(9):934-6
16. Farmer H, McCabe N, Lord CJ, Tutt AN, Johnson DA, Richardson TB, Santarosa M, Dillon KJ, Hickson I, Knights C, Martin NM, Jackson SP, Smith GC, Ashworth A.: Targeting the DNA repair defect in BRCA mutant cells as a therapeutic strategy. Nature. 2005 Apr 14;434(7035):917-21.
17. Warren M, Lord CJ, Masabanda J, Griffin D, Ashworth A.: Phenotypic effects of heterozygosity for a BRCA2 mutation. Hum Mol Genet. 2003 Oct 15;12(20):2645-56.

Talk at IAAC2011
Session: Synthetic Lethality; Theory and Practice
Title: Using Synthetic Lethality Approaches to Design Novel Therapeutic

Abstract

Approaches to Cancer Treatment

As the search for suitable cancer drug targets becomes ever more difficult, the need for novel approaches to this problem is becoming more apparent. Although first proposed in the 1940s, it is only recently that the concept of using synthetic lethality (SL) to design new therapeutic approaches is being tested both in the laboratory and in the clinic. Two genes or proteins are synthetic lethal when deficiency in either is compatible with cellular viability but loss of both is not. Where one partner of a synthetic lethal relationship is a tumour suppressor gene that is lost in tumours, the other synthetic lethal partner, once identified, becomes a candidate drug target. Using this approach, we have identified PARP inhibition as being SL with loss of either the *BRCA1* or *BRCA2* tumour suppressor genes and clinical trials testing this approach are now showing considerable promise. Using this and other examples, I will illustrate how the SL approach can be exploited, how novel targets can be identified and how tumour types as diverse as colorectal, breast, prostate and endometrial cancer could be treated using a SL approach.