

## Lay Summary of a Completed Research Project

<b>CCR No and Study Title:</b>	<b>CCR2798:</b> Identification of testicular germ cell tumour susceptibility genes- the UK genetics of testicular cancer study.		
<b>CI and Sponsor names:</b>	CI: Prof Clare Turnbull Sponsor: Institute of Cancer Research		
<b>Study opening date:</b>	31/12/2006	<b>Study closing date:</b>	30/06/2016
<b>Proposal and Objectives:</b>	<ol style="list-style-type: none"> <li>1. To collect a well characterised series of Testicular Germ Cell Tumour (TGCT) patients.</li> <li>2. For each patient we will determine:             <ol style="list-style-type: none"> <li>a. the age and date of diagnosis,</li> <li>b. the tumour type,</li> <li>c. the laterality of disease (laterality describes which side of a paired organ is the origin of the first tumour),</li> <li>d. treatment of TGCT,</li> <li>e. history of other cancers, and</li> <li>f. history of testicular abnormalities.</li> </ol> </li> <li>3. To obtain blood samples and tumour tissue from each TGCT patient.</li> <li>4. To perform a full and appropriate molecular analysis on all TGCT cases collected, utilising genetic sequencing technologies.</li> <li>5. To identify TGCT susceptibility genes – these are genes that increase the likelihood of developing TGCT.</li> </ol>		
<b>Main Findings:</b>	<ul style="list-style-type: none"> <li>• Samples were collected from 8,180 patients – the largest series of samples from men with TGCT in the world.</li> <li>• We were able to generate significant insights into the heritable genetic basis of TGCT, including:             <ul style="list-style-type: none"> <li>○ TGCT is one of the most strongly heritable common cancers.</li> <li>○ We identified a number of the heritable genetic factors involved in TGCT. These factors comprise both common, low penetrance gene changes and rare, high penetrance gene changes.</li> </ul> <p>Penetrance describes the likelihood of developing a disease from a particular gene change.</p> <p>78 common, low penetrance gene changes have been identified which increase the likelihood of developing TGCT by only a small</p> </li> </ul>		

	<p>amount, but are frequent in the general population. The more of these gene changes a person has, the higher their risk. The UKTGCS sample series were used for identification of ALL of those 78 gene changes: for about half of them we led the study at ICR and for about half we collaborated with international groups.</p> <p>We also identified some very rare, high penetrance, gene changes associated with developing TGCT. These gene changes are extremely uncommon in the general population and each of them only account for small numbers of TGCT cases. There is no single gene strongly associated with TGCT in the way that BRCA1/BRCA2 are associated with breast cancer</p> <ul style="list-style-type: none"> <li>• Tumour analyses were also performed to see if any particular genes were involved in causing TGCTs to be resistance to platinum chemotherapy.             <ul style="list-style-type: none"> <li>○ TGCT is usually highly treatable with platinum-based therapies, however, patients with tumours that are resistant to these therapies have a much poorer outcomes.</li> <li>○ Some patterns of gene change were more common in platinum-resistance tumours, but no single gene was identified to be implicated in platinum-resistance.</li> </ul> </li> </ul>
<p><b>Implications for practice/future research:</b></p>	<ul style="list-style-type: none"> <li>• Testicular cancer is a highly heritable cancer ongoing analysis of which will increase our understanding of the specific genetics basis.</li> <li>• Platinum resistance in testicular cancer remains poorly understood: better understanding of platinum resistance/sensitivity in TGCT will enable improved treatment for men with platinum-resistant TGCT but may also offer insights into why patients with other cancer types respond differentially to platinum chemotherapy.</li> </ul>
<p><b>Dissemination Plan:</b></p>	<p>As per the study protocol, no individual results were made available from this study and participants can be made aware of significant results by contacting the study team. Analyses of samples collected through this study have generated 33 scientific publications. All publications are freely available via the ICR library.</p> <p>Dissemination of findings has also been completed via the Funders (Movember): <a href="#">Movember - Story - Testicular Cancer: Major Study Findings</a> and additional media/communications work has been completed. For example:</p> <ul style="list-style-type: none"> <li>• <a href="#">Science Talk - 'Humphrey' helps unravel the genetics of testicular cancer - The Institute of Cancer Research, London (icr.ac.uk)</a></li> <li>• <a href="https://www.cangene-canvaruk.org/post/investigator-focus-prof-clare-turnbull-and-germ-cell-testicular-cancer">https://www.cangene-canvaruk.org/post/investigator-focus-prof-clare-turnbull-and-germ-cell-testicular-cancer</a></li> </ul>