

D2.4

A complete catalogue of targeted profiles

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Executive Summary

We hereby present the complete catalogue of targeted profiles in WP2 “Identification of sub-clonal genomic alterations”. We used targeted sequencing, OncoScan copy number arrays, and SWATH-MS to profile prostate cancers. In total, 94 tumour samples were profiled using targeted sequencing, 85 samples were profiled for copy number alterations, and 82 samples were profiled for protein expression. Of these, 67 tumour samples were profiled for mutations, copy number alterations, and protein expression. These included samples from with 5 patients using at least 5 regions per tumour and at multiple time points. We used these 67 samples to infer clonality and predict the effects of tumour subclone specific mutations on protein expression. The remaining samples are available for prospective testing of inference methods, as proposed in Tasks 2.1 “Profiling selected PC driver loci” and 2.2 “Ultra-deep profiling of prognostic biomarkers in selected proCOC and MetaProC samples”.

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Chapter 1 Introduction

In WP2, we aimed to investigate whether multi-region genetic profiles could help infer initiating clones, and clones that are associated with increased proliferation and drug resistance. Towards this goal, we profiled 67 tumour samples for mutations, copy number alterations, and protein expression. An additional 27 tumour samples were profiled to prospectively test these predictions. Mutations and copy-number profiles were used by Chimaera (Manica et al., 2018) to infer mutation frequencies and phylogenies, while protein expression profiles were used to test the effects of mutations on gene expression in task 2.3 and already reported in D2.3. All of these data were made available to the consortium and will be made public within 6 months from the conclusion of the project. The 67 samples with CNA, SNV, and protein expression profiles were used to infer tumour subclones, including initiating subclones, mutations associated with increases in proliferation, and the effects of drugs on each subclone. The remaining samples were profiled to be used within a prospective trial for conclusions associated with predictive biomarkers, including mutations or gene dysregulation that are predictive of poor prognosis.

Chapter 2 Generated Data

As a report is not a convenient way to present the complete catalogue of targeted profiles used in this WP, the profiled samples are described in the following supplementary tables.

Table 1¹: OncoScan and Targeted Sequencing. This table is represented using an Excel spreadsheet with multiple tabs. Tabs describe DNA profiling efforts and profiled samples, including tabs with (1) profiles by Sequence-Tagged Site (STS), (2) sample annotations, (3) samples with STS but not Oncoscan, and (4) samples with Oncoscan profiles but not STS.

Table 2²: Somatic single nucleotide variations (SNVs). All predicted somatic mutations from our STS panel are given, and recurring mutations are highlighted in a separate tab.

Table 3³: Copy number alterations (CNAs). Estimated copy numbers for all genes with detected alterations (Loss Threshold <0.5 or >0.5).

Table 4⁴: Visualization of copy number alterations. This is a folder with a visualization for each profiled sample. A global visualization for each sample is given. An example for patient 1, time point 2, region 3 (P1_2_3), is given in Figure 1.

Table 5⁵: This table includes a spreadsheet with all protein expression profiles by UniProt IDs for each sample.

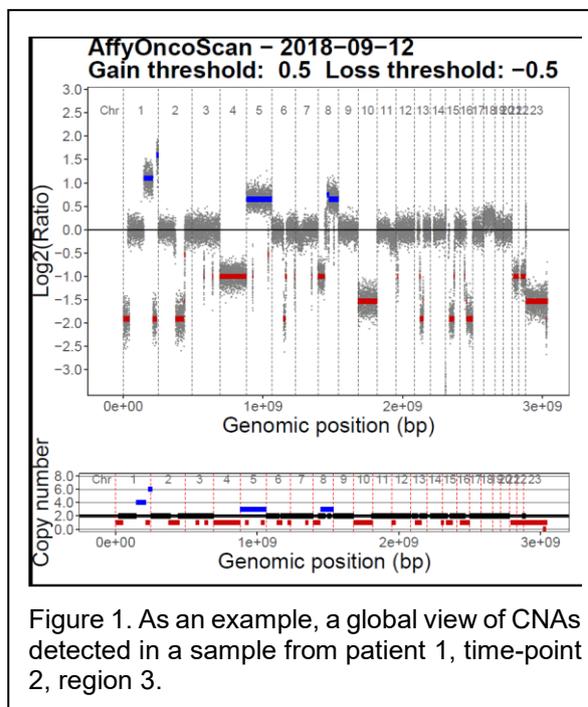


Figure 1. As an example, a global view of CNAs detected in a sample from patient 1, time-point 2, region 3.

¹ Confidential document: PrECISE-D2.4-Table1-OncoScanTargetSeq-Confidential.xlsx

² Confidential document: PrECISE-D2.4-Table2-SNVs-Confidential.xlsx

³ Confidential document: PrECISE-D2.4-Table3-CNAs-Confidential.xlsx

⁴ Confidential document: PrECISE-D2.4-Table4-Visualization-of-copy-number-alterations-CO.zip

⁵ Confidential document: PrECISE-D2.4-Table5-ProteinExpressionProfiles-CO.xls

Chapter 3 Summary and Conclusion

Our analysis of alterations in prostate cancers identified mutations associated with initiating tumour subclones as well as tumour subclones that respond or are resistant to therapies (Manica et al., 2018). Our study demonstrates how tumour profiles that consider multiple areas and time points during tumour evolution can help reveal the ordinal relationship between subclones and their responses to therapies.

Here, we outlined all prostate cancer sample profiles produced to enable tumour-subclone analyses.

Chapter 4 Bibliography

Manica, M., Chouvarine, P., Mathis, R., Wagner, U., Oehl, K., Saba, K., Roditi, L. D. V., Pati, A. N., Martínez, M. R., Wild, P. J., and Sumazin, P. (2018). Inferring clonal composition from multiple biopsies of the same tumor. arXiv, 1701.07940.