Addressing Unmet Clinical Oncology Needs Through A Novel Therapeutic ADC Target Space in Cancer Patient Tissue Biopsies Using OGAP®-Verify

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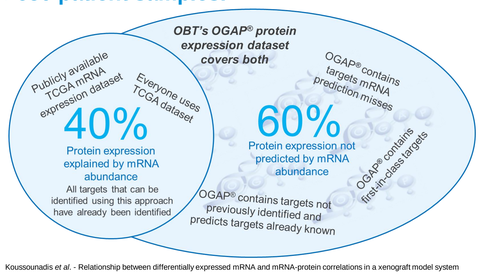
Introduction

Oxford BioTherapeutics (OBT), a leading antibody-drug conjugate (ADC) clinical-stage oncology company, specializing in the identification, validation, and development of first-in-class antibody-based therapeutics utilising its OGAP®-Verify quantitative membrane protein target discovery platform. OBT offers integrated ADC discovery and development, from target discovery through to Investigational New Drug (IND) submission.

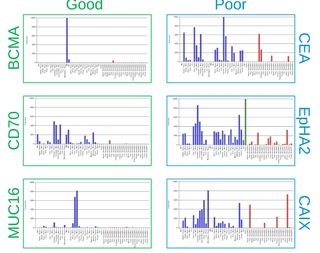
The OGAP®-Verify Discovery Platform

OGAP®-Verify, the world's largest cancer membrane cancer expression databases based on primary patient biopsies is now more sensitive than IHC down to 50 copies per cell. OGAP® measures protein expression directly on patient samples and identifies cancer targets that are otherwise overlooked when using predictive, mRNA-based discovery techniques. **60%** of protein expression does **not** correlate with mRNA expression (Koussounadis *et al.*, 2015) and most targets identified using mRNA are already known. OGAP®-Verify identifies and contains data on membrane proteins in **>650 patient samples.**



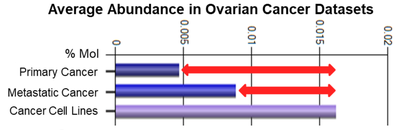
Koussounadis *et al.* - Relationship between differentially expressed mRNA and mRNA-protein correlations in a xenograft model system

Clinical Examples of Targets with High and Low Efficacy Predicted by OGAP®

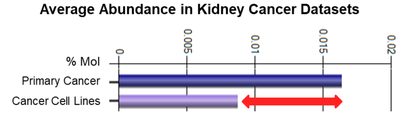


OGAP®-Verify can measure protein abundance (copy numbers per cell) in normal and cancer patient tissues. OBT avoids the ambiguities of ascertaining copy numbers using cell lines, which are not always representative of tissues. The example below highlights the difference in average expression between tissues and cell lines. Cell lines overestimate copy number in ovarian cancer tissues and underestimate copy number in kidney cancer tissues.

Average Abundance in Ovarian Cancer Datasets



Average Abundance in Kidney Cancer Datasets



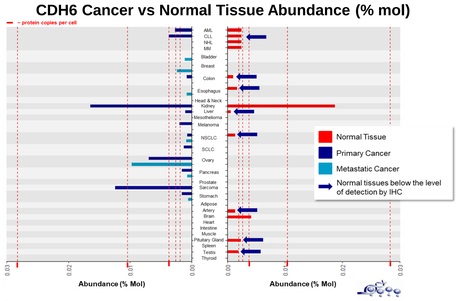
OGAP®-Verify is now more sensitive than IHC, measuring protein expression as low as 50 copies-per-cell allowing us to confidently determine the therapeutic index of cancer targets. OGAP®-Verify avoids some of the ambiguities of IHC in terms of antibody specificity and sensitivity when evaluating normal tissue expression of a therapeutic candidate.

Table Summarising The OGAP®-Verify Detection Rate for Membrane Proteins in Prostate Cell Line PC-3

Protein	Copies per Cell	Protein Detected?
PLEKHG4	39	Y
MTTP	64	Y
LENG8	88	Y
TMEM143	149	Y
FURT3	666	Y
TMEM51	949	N
MAGI1	1686	Y
TMCO4	2097	Y
TMEM132A	3685	Y
TMCC1	4156	Y
TMEM68	5267	Y
OSTM1	5436	Y
PEX11G	6570	Y
SMAP1	6852	Y
TAPT1	7719	Y
PCDHGC3	8122	N
CDH1	9061	Y
TMEM177	10005	Y
PEX16	10342	Y
MPP1	11042	Y
TMEM55A	12942	Y
TM7SF3	13762	Y
TMEM120A	14544	Y
TMEM127	15683	Y
TMEM161B	16870	Y
TMEM56	19885	Y
TMEM181	20072	Y
TMEM165	515859	Y

Mann *and coworkers* - A "Proteomic Ruler" for Protein Copy Number and Concentration Estimation without Spike-in Standards

CDH6 Cancer vs Normal Tissue Abundance (% mol)

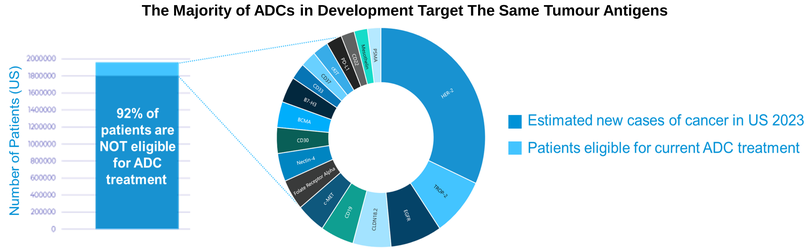


The table above summarises the OGAP®-Verify detection rate in prostate cancer cell line, PC-3. The detection rate reaches as low as 50 copies-per-cell for membrane proteins. The comparative bar chart summarises CDH6 cancer abundance vs normal abundance (% mol). The arrows indicate the normal tissues OBT identified that are below the level of detection by IHC.

ADC Landscape

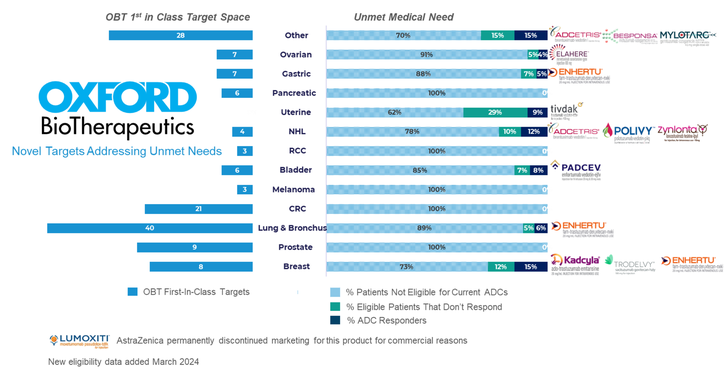
Notwithstanding recent advancements in ADCs, just ~10% of new US cancer patients in 2022 were eligible for treatment with existing ADCs. ADC-target tumor expression is a major factor in patient eligibility. Despite this, most clinical ADCs are directed to the same 9 targets as already approved ADCs.

The Majority of ADCs in Development Target The Same Tumour Antigens



OBT works on first-in-class targets. We develop drugs to treat patients who are currently ineligible for existing treatments.

OBT's First-in-Class Target Space vs Cancer Patient Clinical Unmet Need

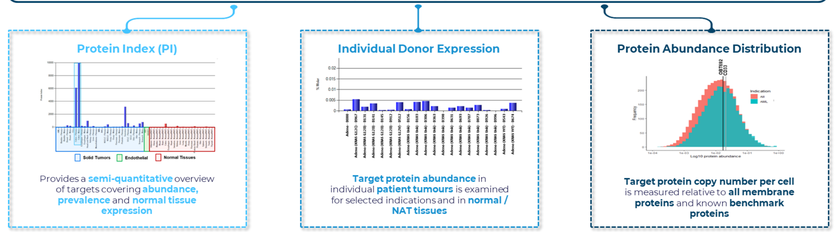


There is sizeable greenspace within the current ADC landscape encompassing: (1) Indications where no suitable target has been identified, (2) Patient populations with no target expression and (3) Patients refractory to existing ADCs. OBT have identified novel targets addressing these unmet needs.

OGAP®-Verify Target Space

OGAP®-Verify target evaluation leverages multiple key target elements: prevalence, individual patient target abundance, target copy numbers in cancer, normal tissues and cell lines. Additionally, the OGAP® cancer cell line PI plot is examined to investigate if cell lines correlate with the cancer indications identified using the tissue PI; OGAP® contains an extensive repository of ~100 cancer cell lines.

Identification *and* ***quantification*** *of nearly* ***all membrane proteins*** *in* ***all patient samples, simultaneously****, covering* ***primary and metastatic*** *tumour samples directly from patients, and* ***NAT / normal tissues*** *from patients, with the* ***number of patient samples*** *currently contained within OGAP® at* ***650 and counting***



OGAP®-Verify can identify novel targets and its validation data substantially de-risks programs before significant investment is made. Maximising chance of success.

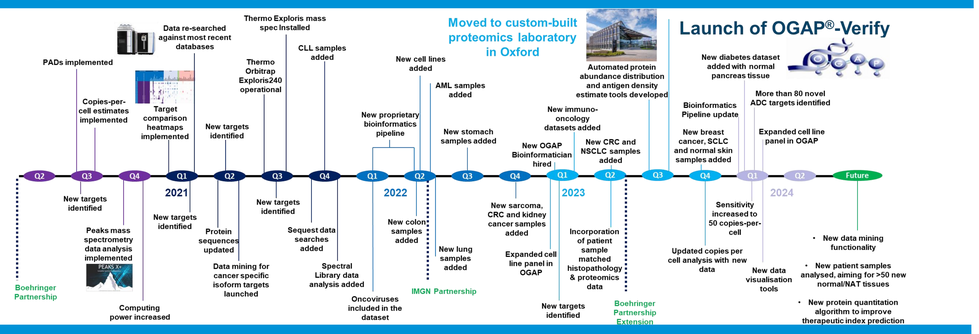
OGAP®-Verify ADC Targets Available for Partnering

Further orthogonal data is collected including literature, public RNA / protein expression data, subcellular localisation, protein structure predictions, clinical trials, patents and freedom to operate, bioinformatic and homology analysis and reagent designs to help frame a highly tailored research plan.

OGAP® Pipeline Development

OGAP®-Verify measures protein expression on patient samples, which is the TRUE target space and therefore can identify novel targets missed by mRNA analysis. We work on first-in-class targets to develop drugs to treat patients who are ineligible for existing treatments

Furthermore, OGAP®-Verify analysis, prior to starting validation or during target selection, avoids wasting time and resources on a program that may not have a good therapeutic index and could fail further downstream in the development process. The OGAP® pipeline is being continually developed, and with that, additional targets are identified.



Conclusion

OGAP®-Verify contains all this data **NOW**, for **EVERY** protein before any investment in wet bench validation. OGAP®-Verify can identify novel targets and substantially de-risks programs at the start, predicting clinical efficacy and toxicities. OGAP®-Verify is more sensitive than IHC, highlighting normal tissue expression concerns at the start and contains antigen density information to aid payload selection and clinical development. OBT's pipeline and development capabilities have been validated through multiple strategic partnerships including Boehringer Ingelheim, ImmunoGen and Genmab. It has yielded 3 clinical stage first-in-class programs and a further 15 first-in-class partnered assets to date. OBT offers integrated ADC discovery and development, from ADC target discovery through to Investigational New Drug (IND) submission and we would be pleased to discuss partnership opportunities.