ContextualGenomics

Find-It™ (CG001) Cancer Hotspot Panel

- ✓ **Over 90 carefully selected clinically actionable cancer mutations in one panel**
- ✓ **From tumour sample to clinical report in seven days**
- ✓ **Guaranteed detection of mutations at 5% allele frequency (VAF) and higher**
- ✓ **Proprietary pipeline developed and maintained by a team of world-renowned cancer scientists**
- ✓ **Unsurpassed quality control to ensure accuracy of results**

The Contextual Genomics Find-It (CG001) Cancer Hotspot Panel is a multiplex, genomic assay designed for next- generation sequencing. Find-It takes the user through from tumour sample to clinical report detecting common, clinically actionable genomic alterations in solid tumours including single base substitutions, small deletions and insertions.

Find-It simultaneously evaluates the mutation status of tumour DNA at approximately 90 well-characterized positions and several exons in 29 cancer associated genes. Median depth of coverage at these hotspots is 15,000 X. Mutations include SNVs and short indels (max 24bp), which were carefully selected by Contextual Genomics' team of cancer scientists and physicians. Mutations on the Find-It panel are therefore relevant to standard of care treatment, including treatment resistance, as well as to currently available clinical trials that may be of potential value to the patients' treatment plan. 45% of the panel is relevant to on or off-label available drugs, and 76% is relevant to available drugs or clinical trials. The remaining 24% of the panel contains resistance mutations and positions selected by advisors from the pharmaceutical industry **(Table 1).**

The ability of Find-It to detect common, actionable mutations is coupled with unprecedented seven-day turn-around-times and comprehensive reporting. Reports feature a detailed clinical interpretation and recommendations based on the mutation profile of the tumour, and are generated both for the physician and the patient. This seamless, full-service approach may allow physicians to make more informed treatment decisions and potentially offer patients the most current cancer management plan available.

Sample requirement specifications

Suitable samples include FFPE blocks, scrolls, cores and unstained slides. All samples should have a minimum of 10% nuclear tumour content. FFPE blocks should have a minimum of 1cm x 1cm tissue content. Scrolls, cores and slides must be accompanied by H&E or digital image.

Gene	Mutation	On label drugs	Off-label drugs	Clinical trials	Resistance
AKT1	E17			■	
ALK	T1151, L1152, C1156, F1174, L1196, G1269, R1275		■	■	■
AR	S741, W742, H875, Q876, T878				■
BRAF	Q201, G466, G469, Y472, D594, G596, L597, V600	■	■	■	■
CDKN2A	R58			■	
CTNNB1	S37, T41, S45		■		
EGFR	exons 18, 19, 20, 21	■	■	■	■
ERBB2	G309, S310		■		
ESR1	V534, P535, L536, Y537, D538		■		■
FGFR1	N546, K656				
FGFR2	S252, P253, N549, K659			■	
GNA11	Q209			■	
GNAQ	Q209			■	
GNAS	R201				
HRAS	G12, G13, Q61			■	
IDH1	R132			■	
IDH2	R140, R172			■	
JAK1	V658, S703				
KIT	D816, D820, N822, Y823, exons 11, 13		■	■	■
KRAS	G12, G13, Q61, K117, A146	■	■	■	■
MAP2K1	Q56, K57, K59, D67, P387				■
MAP2K2	F57, Q60, K61, L119				
MET	Y1253, exons 13, 18				
NRAS	G12, G13, Q61, K117, A146	■		■	
PDGFRA	D842		■	■	■
PIK3CA	E542, E545, Q546, D549, M1043, N1044, A1046, H1047, G1049		■	■	■
PTEN	R130, R173, R233		■	■	■
RET	C634, M918		■	■	
STK11	Q37, P281, F354			■	

Table 1: Mutations present on the Find-It panel and their implications for treatment.

Contextual Genomics Inc.
Suite 204 – 2389 Health Sciences Mall,
Vancouver, British Columbia, V6T 1Z3

ContextualGenomics

Contextual Genomics Bioinformatics and Genome Analytics Pipeline (CGBP) v2.2.1

Contextual Genomics has developed a robust, accurate and high-throughput bioinformatics system for the identification and clinical interpretation of mutations from targeted next-generation sequencing (NGS) data using the Find-It panel. The central component of this system is the bioinformatics and genome analytics pipeline (CGBPv2.2.1). The CGBPv2.1.1 pipeline has been rigorously validated using large cohorts of tumour samples, as well as commercially available cell line controls, with available orthogonal data. The pipeline has demonstrated high accuracy with sensitivity and specificity >99.9% **(Table 2).**

Table 2	Sensitivity	Accuracy	PPV	Cohort size	LOD (VAF%)
Indels	1	1	1	53	1%
SNV's	0.9912	0.9998	1	198	3%
95% CI	0.973 - 0.998	0.9998 - 0.999			

Table 2: Sensitivity, specificity, accuracy, positive predictive value (PPV), and limit of detection (LOD) of the Find-It Panel for single nucleotide variants (SNV's) and indels.

Reproducibility and Repeatability

Experiments to investigate reproducibility and repeatability have shown correlations of allele frequency (VAF) at >0.99 and >0.98 within and between runs respectively, for both SNVs and indels. Furthermore, reproducibility has been assessed at 100% of mutations detected compared to orthogonal data. This includes comparisons between sequencing runs, laboratory technologists, MiSeq® instruments, days, and DNA extractions using 76 samples.

Limit of Detection (LOD)

Although Find-It currently reports mutations at or above 5% VAF, droplet digital (dd)PCR has validated the ability of the Find-It panel to accurately identify mutations with VAF as low as 0.47%.

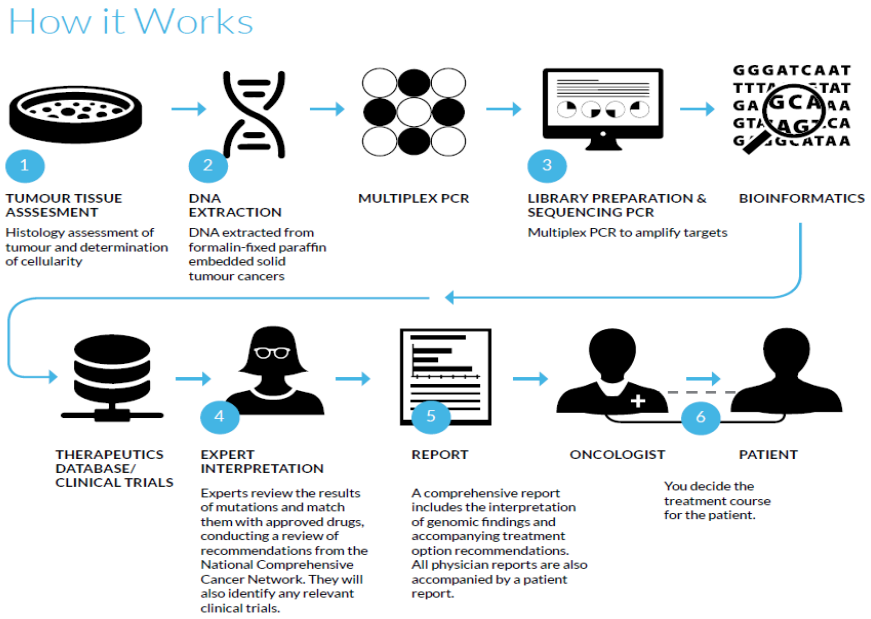

Figure 1: The Find-It panel work- flow from sample extraction, library prep, sequencing, variant calling, interpretation, to clinical reporting.