

clara^T Technical Specification

Research Use Only

clara^T is a unique software-driven solution classifying biologically relevant gene expression signatures into a comprehensive, easy to interpret report.

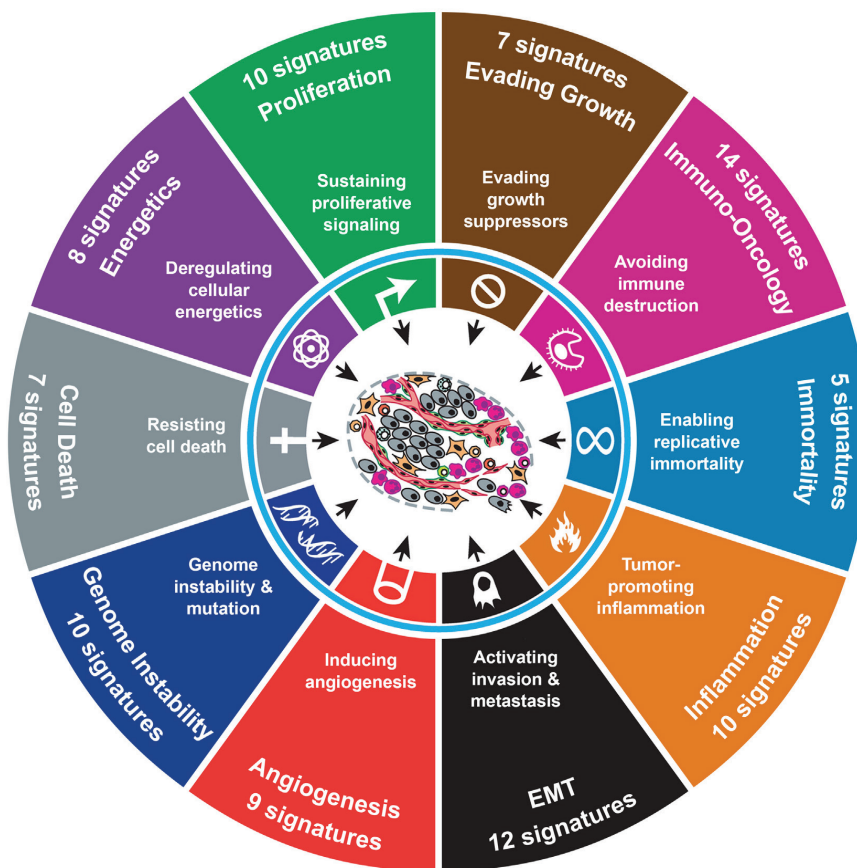


Image adapted from The Hallmarks of Cancer. Originally published in Cell 144, Hanahan D & Weinberg RA, Hallmarks of Cancer: The Next Generation, 646-674, © 2011. With permission from Elsevier.

| Immuno-Oncology | Signature name | Associated publications | Brief description |
|--|--|--|---|
| | Almac I-O Assay | Mulligan et al. 2014. Parkes et al. 2017 | c-GAS-STING biology |
| | TILs Exhausted T-cells | Danaher et al. 2017 | Immune cell populations |
| | TILs-related GS | Kochi et al. 2018 | Lymphocytic infiltration |
| | T-cell inflamed GEP* | Ayers et al. 2017 | T-cell inflamed IFN γ response genes |
| | IPRES Signature | Hugo et al. 2016 | Innate anti-PD-1 resistance genes |
| | TCGA CSF1 Signature* | Beck et al. 2009 | Macrophage-CSF1 response genes |
| | TCGA Lymphocyte Signature* | Calabro et al. 2009 | Lymphocyte infiltration associated genes |
| | TCGA TGF β Signature* | Teschendorff et al. 2010 | TGF β signalling genes |
| | TCGA IFN γ Signature* | Wolf et al. 2014 | IFN γ signalling genes |
| | TCGA Fibroblast CSR* | Chang et al. 2004 | Wound healing signature |
| | TGF β Response Signature | Mariathasan et al. 2018 | TGF β signalling genes |
| | CTLA4 Response Signature | Ji et al. 2011 | IFN γ and Th1-associated genes |
| | Immune Response (T-cells) | Prat et al. 2017 | Immune cell populations |
| Immune Enrichment Score* | Miao et al. 2018. Liberzon et al. 2015 | IFN γ Hallmark Geneset | |
| Single Gene Targets | | | |
| CTLA4, PDL1, PD1, LAG3, TIM3, OX40, ICOS, CD27, CD40, IDO1 | | | |

| Epithelial to Mesenchymal Transition | Signature name | Associated publications | Brief description |
|--|--------------------------|-------------------------|---|
| | Almac EMT Assay | Knight et al. 2018 | Subgroup driven by EMT/MAPK signalling |
| | MPI Signature | Gentles et al. 2015 | Tumour/Stromal genes |
| | MCPCounter-Fibroblasts | Becht et al. 2016 | Stromal genes and cell counterparts |
| | MAPK Activity Score | Wagle et al. 2018 | MAPK signalling pathway |
| | EMT Signature Estimate | Tan et al. 2014 | Epithelial & Mesenchymal response genes |
| | Pan-Can EMT Signature A | Rokavec et al. 2017 | EMT-induced genes, RBM47 downregulation |
| | MEK Functional Signature | Dry et al. 2010 | Genes predicting MEK addiction |
| | EMT Signature* | Byers et al. 2013 | EGFR and P13K/AKT response genes |
| | EMT-based GE Signature* | Schell et al. 2016 | RAS signalling genes |
| | Mesenchymal Subtype | Lee et al. 2017 | Subgroup driven by EMT/MAPK signalling |
| | Pan-Can EMT Signature B | Mak et al. 2016 | EMT correlated markers e.g. AXL |
| EMT Enrichment Score* | Liberzon et al. 2015 | EMT Hallmark Geneset | |
| Single Gene Targets | | | |
| AXL, FAK1, NOTCH1, EGFR, BRAF, KRAS, MET, TGF β , FGFR1, FGFR2 | | | |

| Inflammation | Signature name | Associated publications | Brief description |
|---|---------------------------------------|-------------------------------|---|
| | NFκB Activity Signature | Hopewell et al. 2013 | NFκB signalling and immune surveillance |
| | IKKβ Signature* | Hernandez et al. 2010 | NFκB and IKKβ signalling genes |
| | Tumour-associated Macrophages* | Steidl et al. 2010 | Classification of CD68+ macrophages |
| | M1/M2 GE Signature | Yuan et al. 2015 | Classification of M1/M2 macrophages |
| | IL1β Signature* | Wu et al. 2018 | IL1β signalling and immunomodulation |
| | TILs Macrophages | Danaher et al. 2017 | Immune cell populations |
| | TCGA CSF1 Response* | Beck et al. 2009 | Macrophage-CSF1 response genes |
| | TCGA Wound Healing* | Chang et al. 2004 | Wound healing signature |
| | Immune Response (Macrophages) | Prat et al. 2017 | Immune cell populations |
| Inflammatory Response Enrichment* | Liberzon et al. 2015 | Inflammation Hallmark Geneset | |
| Single Gene Targets | | | |
| NFκB, STAT5, STAT2, JAK2, CCL2, CXCL8, TNFα, IL1β, IL2, IL6 | | | |

| Genome Instability | Signature name | Associated publications | Brief description |
|---|-----------------------------------|--|---|
| | Almac DNA Damage Assay | Mulligan et al. 2014. Parkes et al. 2017 | DNA damage induced immune response |
| | HRD Gene Signature* | Peng et al. 2014 | Molecular HR repair functional network |
| | BRCAness Profile | Konstantinopoulos et al. 2010 | Platinum resistance & DNA repair genes |
| | BRCA1ness Signature | Severson et al. 2017 | DNA replication, recombination & repair |
| | DNA Damage Sensitivity | McGrail et al. 2017 | PARPi responsive and sensitive genes |
| | CIN25 Signature | Carter et al. 2006 | Genome integrity maintenance |
| | CIN4 Signature | Szasz et al. 2013 | Tumour aneuploidy status |
| | DDR Pathway Focused Score* | Kang et al. 2012 | Platinum-induced DNA damage repair |
| | MSI Classifier* | Kruhoffer et al. 2005 | MSI or MSS gene expression patterns |
| DDR Enrichment Score* | Liberzon et al. 2015 | DNA Damage Hallmark Geneset | |
| Single Gene Targets | | | |
| BRCA1, BRCA2, ERCC1, ATR, ATM, PARP1, WEE1, CHK1, CHK2, DNAPK | | | |

| Proliferation | Signature name | Associated publications | Brief description |
|---|------------------------------------|---------------------------|--|
| | ERBB2-specific GES* | Bertucci et al. 2004 | ERBB2 +/- discriminator genes |
| | pSTAT3-GS Score | Sonnenblick et al. 2015 | Constitutive activation of STAT3 |
| | EGFRi67 Gene Signature* | Goodspeed et al. 2018 | TKI signalling and response signature |
| | EGFR Sensitivity Signature* | Balko et al. 2006 | Mechanisms of aberrant EGFR signalling |
| | KRAS Dependency Signature | Singh et al. 2009 | Genes predicting KRAS addiction |
| | HER2i Sensitivity Score | McGrail et al. 2017 | HER2i responsive and sensitive genes |
| | MYC Activity Signature | Jung et al. 2016 | MYC regulated gene network |
| | MAPK Activity Score | Wagle et al. 2018 | MAPK signalling pathway |
| | MEK Functional Signature | Dry et al. 2010 | Genes predicting MEK addiction |
| PI3K/AKT Enrichment Score* | Liberzon et al. 2015 | PI3K/AKT Hallmark Geneset | |
| Single Gene Targets | | | |
| HER2, ESR1, PI3K, IGF1R, AKT, MEK1, ERK, SRC, EGFR, PGR | | | |

| Angiogenesis | Signature name | Associated publications | Brief description |
|--|---------------------------|-------------------------------|--|
| | Almac Angio Assay | Gourley et al. 2014 | Anti-angiogenic signature |
| | Angiogenesis Signature A* | Hu et al. 2005 | Vascular re-modelling and integrins |
| | MTTS Signature | Glinsky et al. 2005 | BMI-1 driven pathway |
| | Angio/Hypoxia Signature | Franzini et al. 2015 | Hypoxia response pathway |
| | Vascular Proliferation | Stefansson et al. 2015 | Microvessel proliferative signalling |
| | Global Angio Signature* | Anders et al. 2013 | Correlated angiogenic genes |
| | Angiogenesis Signature B* | Bentink et al. 2012 | Angiogenic vs Non-angiogenic subgroups |
| | Angio Predictive G Model | Mendiola et al. 2016 | Anti-angiogenic response genes |
| Angio Enrichment Score* | Liberzon et al. 2015 | Angiogenesis Hallmark Geneset | |
| Single Gene Targets | | | |
| VEGFA, VEGFR1, VEGFR2, PDGFR1, PDGFR2, ANG1, ANG2, PIGF, NDRG1, cKIT | | | |

| Energetics | Signature name | Associated publications | Brief description |
|--|---------------------------------------|---------------------------|---|
| | GLS1/GCS Co-Dependency Signature | Daemen et al. 2018 | GLS1 inhibition sensitivity genes |
| | Glycolytic GS Signature (GGESS) | Chen et al. 2017 | Glycolysis and IDH1 associated genes |
| | Glycolysis-related Signature | Liu et al. 2019 | Glycolysis related genes |
| | Core Metabolic Signature* | Haider et al. 2016 | Metabolic shift associated with hypoxia |
| | Hypoxia-related Signature | Yang et al. 2018 | Regulatory module of hypoxia genes |
| | Metabolic Pathway Signature* | Von-Rundstedt et al. 2016 | Altered metabolic pathways |
| | Metabolic Progression Signature* | Nath et al. 2016 | Lipogenesis and fatty acid metabolism genes |
| | Oxidative Phosphorylation Enrichment* | Liberzon et al. 2015 | Oxidative Phosphorylation Hallmark Geneset |
| Single Gene Targets | | | |
| TXNIP, GLUT1, MYC, IDH1, FASN, AMPK, HIF1 α , mTOR, PRDX1, SOD1 | | | |

| Evading Growth | Signature name | Associated publications | Brief description |
|--|-----------------------------------|-------------------------|--|
| | Cell Cycle Signature (CCS) | Mizuno et al. 2009 | Cell cycling and non-cycling genes |
| | E2F Target Expression Classifier* | Lan et al. 2018 | E2F highly and lowly dependent genes |
| | CDK4 Classifier | Raspe et al. 2017 | Predicts phosphorylation status of CDK4 |
| | RB-1 Loss Signature* | Chen et al. 2019 | RB1 bi-allelic loss and pathway disruption |
| | E2F Gene Signature* | Locatelli et al. 2010 | E2F biomarker of CDK inhibitor activity |
| | TP53 Classifier | Knijnenburg et al. 2018 | TP53 target genes and deficiency |
| | G2M Checkpoint Enrichment* | Liberzon et al. 2015 | G2M Checkpoint Hallmark Geneset |
| Single Gene Targets | | | |
| CDK1, CDK2, CCND1, CCNE1, FOXM1, WEE1, TP53, RB1, CHK1, CHK2 | | | |

| | Signature name | Associated publications | Brief description |
|---|---|-------------------------|---|
| Cell Death | TRAIL Sensitivity Predictor | Chen et al. 2012 | IFN and MHC induced genes |
| | TNFα-based GE Signature* | Bardia et al. 2018 | Genes linked to an IAP biology |
| | Tumour Necrosis Signature | Bredholt et al. 2015 | HIF1A, NF- κ B and P13K/mTOR genes |
| | Apoptosis Pathway (APS) | Chang et al. 2015 | Apoptosis pathway specific genes |
| | Autophagy-related Risk Score | An et al. 2018 | Autophagy-related phenotype expression |
| | TP53 Classifier | Knijnenburg et al. 2018 | TP53 target genes and deficiency |
| | Apoptosis Enrichment Score* | Liberzon et al. 2015 | Apoptosis Hallmark Geneset |
| Single Gene Targets | | | |
| MCL, BCL2, MDM2, BAX, IAP1, IAP2, BAD, BID, Survivin, cFLIP | | | |

| | Signature name | Associated publications | Brief description |
|---|---|------------------------------|---|
| Immortality | Universal Senescence Signature* | Hernandez-Segura et al. 2017 | Specific senescence-induced stress & cell types |
| | Telomerase (Terc) Signature* | Bruedigam et al. 2014 | Telomerase inhibition and tumour depletion |
| | Molecular Senescence Signature* | Marques et al. 2017 | Novel candidates of cellular senescence |
| | Senescence-associated Signature* | Purcell et al. 2014 | Senescence associated secretory phenotype |
| | Candidate Senescence Signature* | Wu et al. 2019 | Regulators of p21-induced senescence |
| Single Gene Targets | | | |
| TERT, RB1, p21, p16, TP53, Ki67, MDM2, E2F1, TRF1, POT1 | | | |

Signatures within the clara^T report have been reviewed and implemented based on information from the publications. Based on limited information, signatures denoted with an (*) have been implemented with some modifications to those described in the relevant publications. Signatures implemented with an adapted methodology use a standardised approach to average gene expression across samples. For further details on each gene signature please refer to the relevant publications. Reference to the publications is not intended to direct the Customer towards particular uses of the signature scores. Single genes within the clara^T report have been selected as analytes relevant to each biology based on the Molecular Signatures Database Hallmark Gene Sets (Liberzon et al. 2015; Copyright ©2004-2017 Broad Institute Inc. and subject to the terms and conditions of the Creative Commons Attribution 4.0 International License).

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