CHRONIC MYELOID LEUKEMIA HSC (haematopoietic stem cell) Haematopoietic stem cell Apoptosis K02158 Survival PI3K-Akt signaling pathway +p ►O — — ► Survival, Proliferation K04438 → Survival K07293 CMP (common myeloid K06624 CLP Proliferation (common lymphoid progenitors) K02833... ─► Proliferation progenitors) DNA MAPK signaling pathway GMP (granulocyte/ **▶**○ → ? macrophage progenitors) DNA K11223... T Survival DNA (B cell/ T cell) Granulocyte CML-CP (chronic phase of chronic myeloid leukemia) K06621 Cell cycle Ò DNA Genetic alterations K06625 BCR-ABL, EVI-1, AML-EVI1 Oncogenes: K02089... Tumor suppressors: INK4a/ARF, p53, Rb Hematopoietic cell lineage K06621 ►G1/S progression DNA Blast crisis Karyotypic instability Impaired G1 cycle arrest Reduced apoptosis p53 signaling pathway DNA. damage DNA K04462... TGF-β signaling pathway +p Smad3 K04674 Abnormality in growth inhibition K13375... K04388 DNA CML-BP (blast phase of CML) (Myeloid) K04501 CML-BP (Lymphoid)

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