SUPPLEMENTARY FIGURE AND TABLE LEGENDS

Supplementary Figure 1. Cbl follows similar temporal course of phosphorylation as GMRβc upon GM-CSF treatment. Serum starved HEK293 cells transfected with the indicated plasmids treated with or without 1 ng/ml of GM-CSF for indicated time points, were lysed and immunoprecipitated with anti-GMRβc or anti-HA antibody and immunoblotted with anti-pTyr antibody. IP: immunoprecipitation.

Supplementary Figure 2. Dasatinib inhibits growth of primary JMML cells from patients with CBL, NF1, NRAS, or PTPN11 mutation in a dose dependent manner. (A) Individual JMML patient-derived leukaemic cells with the indicated mutations (see **Supplementary Table 1**) were exposed to increasing concentrations of dasatinib in the absence or presence of GM-CSF (10 ng/mL). Percent maximum colony growth is graphed in relation to 0 nM dasatinib at 10 ng/mL of GM-CSF. **(B)** Cell number per colony and cell size plated from a patient harbouring a Cbl(C396R), N-Ras(G12D) mutation or NF1 LOH significantly decreased in the presence of increasing concentrations of dasatinib with and without GM-CSF. Colonies were visualized at a total magnification of 40X on a 2 mm-grid dish.

Supplementary Figure 3. Dasatinib, but not imatinib, markedly inhibits JMML colony formation in the absence or presence of GM-CSF. (A) A comparison of percent maximal colony growth for samples (n=5) in 0 ng/mL of GM-CSF without and with dasatinib at 150 nM was statistically significantly different using a paired t-test (P=0.0026) as was the comparison for the same 5 samples in 10 ng/mL of GM-CSF (P=0.002). Error bars are depicted for S.E.M at each concentration. **(B)** JMML samples (n=3: HM3397, HM3526 and HM3541) and one normal bone marrow sample (HM3515) were exposed to two different concentrations of imatinib (1 uM and 10 uM) without and with GM-CSF, and represented individually (top graph) or as an

average of three JMML samples (bottom graph). No differences in growth inhibition were observed regardless of the presence of GM-CSF (two-tailed P-value=0.1738).

Supplementary Figure 4. Dasatinib inhibits GM-CSF-induced phosphorylation of ERK in primary JMML cells from patients with CBL, NF1 and PTPN11 mutation. (**A)** Primary peripheral mononuclear cells collected from a patient with a Cbl(Y371H) mutation were stimulated with or without GM-CSF in the presence or absence of 50 or 150 nM of dasatinib. Cell lysates were then prepared and immunoblotted with the indicated antibodies. **(B)** Primary peripheral mononuclear cells collected from a patient with a Cbl intron 8 deletion were stimulated with or without GM-CSF in the presence or absence 150 nM of dasatinib and cell lysates were blotted with indicated antibodies. **(C)** Primary peripheral mononuclear cells collected from a patient with a PTPN11(E76V) mutation were stimulated with or without GM-CSF in the presence or absence of 50 or 150 nM of dasatinib. Cell lysates were then prepared and immunoblotted with the indicated antibodies. **(D)** Primary peripheral mononuclear cells collected from a patient with a NF1 LOH were stimulated with GM-CSF in the presence or absence of 150 or 250 nM of dasatinib and cell lysates were immunoblotted with indicated antibodies.

Supplementary Table 1. JMML patient-derived primary cell information. The mutational and disease status, as well as the colony assay results are indicated for the noted primary leukaemic cells collected from either the peripheral blood (PB) or bone marrow (BM).