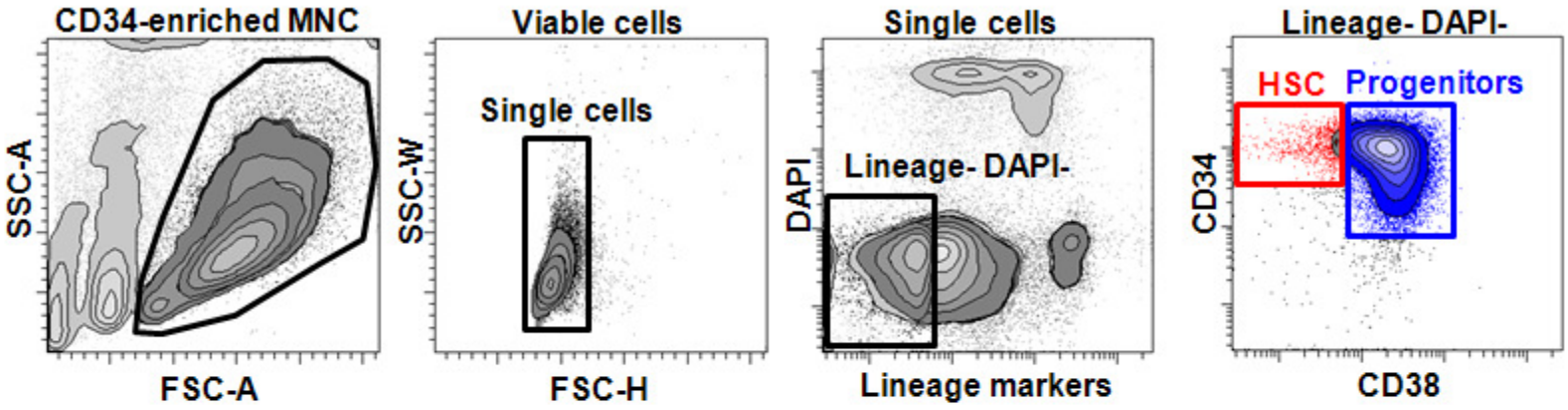
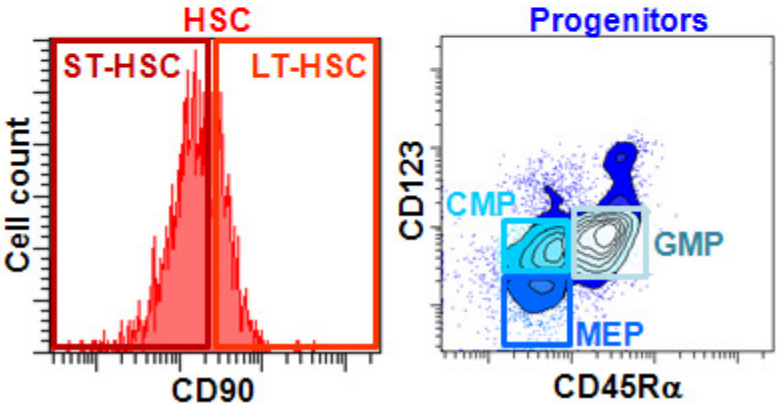
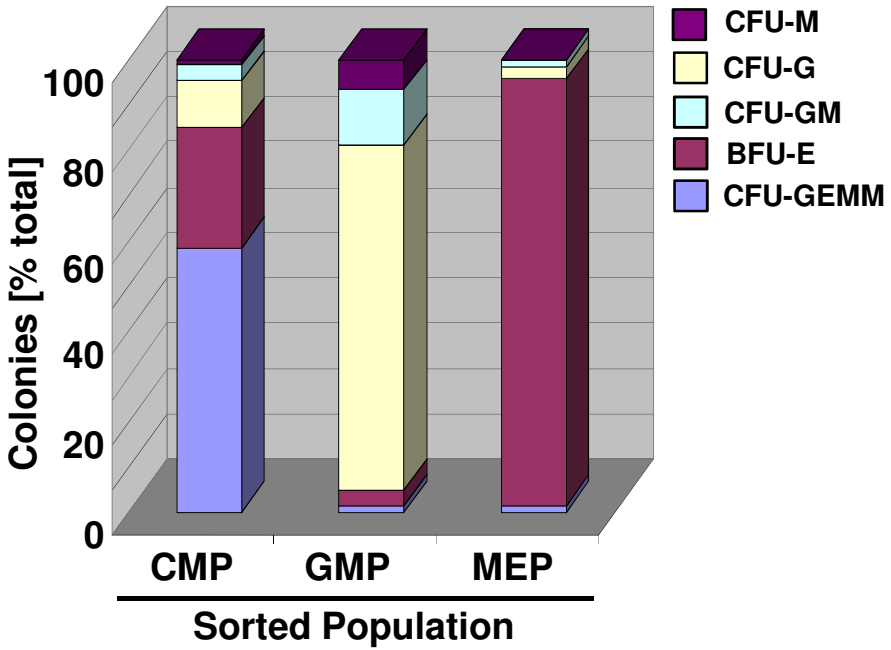


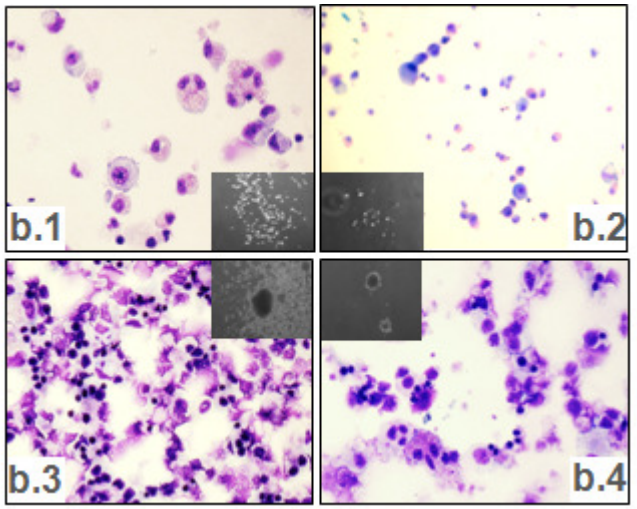




**S1: Sorting strategy for the isolation of hematopoietic stem and myeloid progenitor cells from the bone marrow or peripheral blood from healthy controls and patients with MDS.** CD34+ cell-enriched bone marrow or peripheral blood mononuclear cells were analyzed for the expression of lineage markers. Cells not expressing lineage markers were separated into five subpopulations: Long-term hematopoietic stem cells (LT-HSC: Lin-CD34+CD38-CD90+), short-term hematopoietic stem cells (ST-HSC: Lin-CD34+CD38-CD90-), common myeloid progenitors (CMP; Lin-CD34+CD38+CD123+CD45RA-), granulocyte-monocyte progenitors (GMP; Lin-CD34+CD38+CD123+CD45RA+) and megakaryocyte-erythrocyte progenitors (MEP; Lin-CD34+CD38+CD123-CD45RA-).

A

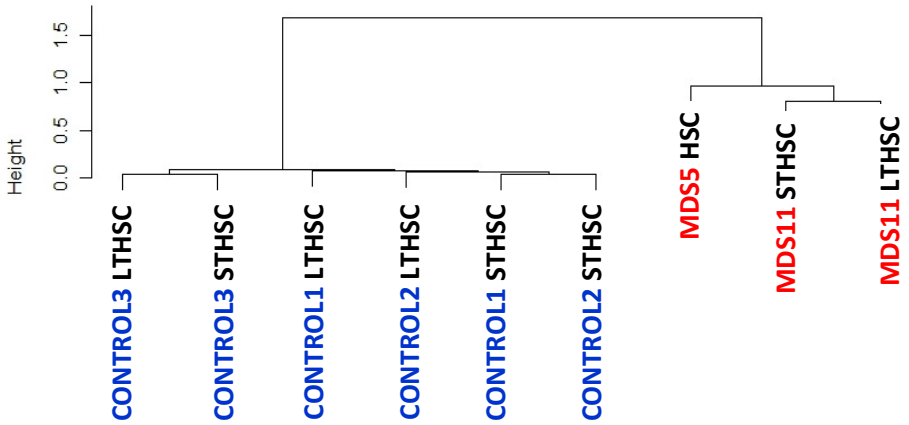



B



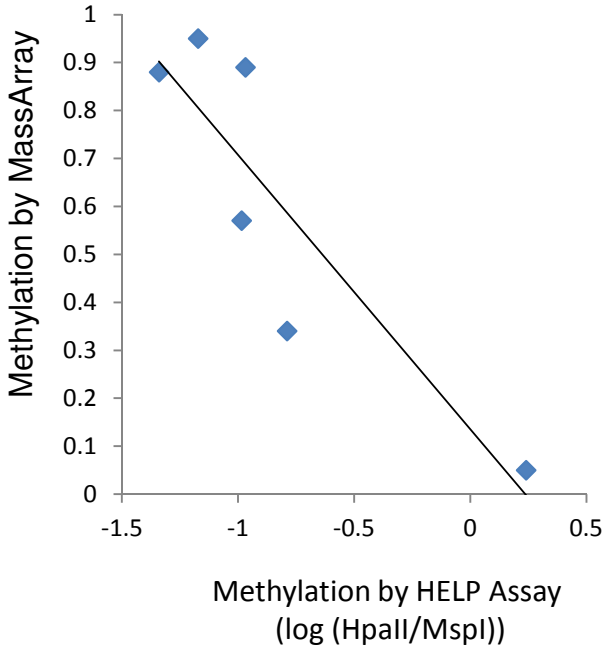

**S2: Functional confirmation purified hematopoietic progenitor populations using methylcellulose assays to test clonogenic capacity.** Bone marrow derived common myeloid progenitors (CMP; Lin-CD34+CD38+CD123+CD45RA+-), granulocyte-monocyte progenitors (GMP; Lin-CD34+CD38+CD123+CD45RA+) and megakaryocyte-erythrocyte progenitors (MEP; Lin-CD34+CD38+CD123-CD45RA-) were FACS-sorted and seeded in semisolid medium containing cytokines (Stem Cell Technologies, #H4434 GF+). Differential colony counts 14 days after seeding of 500 sorted progenitor cells showed an efficient separation of MEP, GMP and CMP. While the majority of CMP contained immature mixed colony-forming units (CFU-GEMM, colony-forming unit- granulocyte-erythrocyte-monocyte megakaryocyte), as well as all other more lineage-restricted progenitors: erythroid (BFU-E), granulocytic-monocytic (GFU-GM), CFU-granulocytic (CFU-G) and monocytic (CFU-M). GMP contained predominantly CFU-G, GM, and M progenitor cells but only a few CFU-GEMM or BFU-E initiating cells. MEP gave rise to predominantly BFU-E and marginal numbers of the other lineages (A). Colony morphology and cell morphology (cytospin) of isolated, individual colonies (B): b.1 CFU-G containing granulocytes, b.2 CFU-GM containing granulocytes and monocytes, b.3 GEMM comprising all myeloid cell types and b.4 BFU-E containing erythroid cells.

**Supp Fig 3**



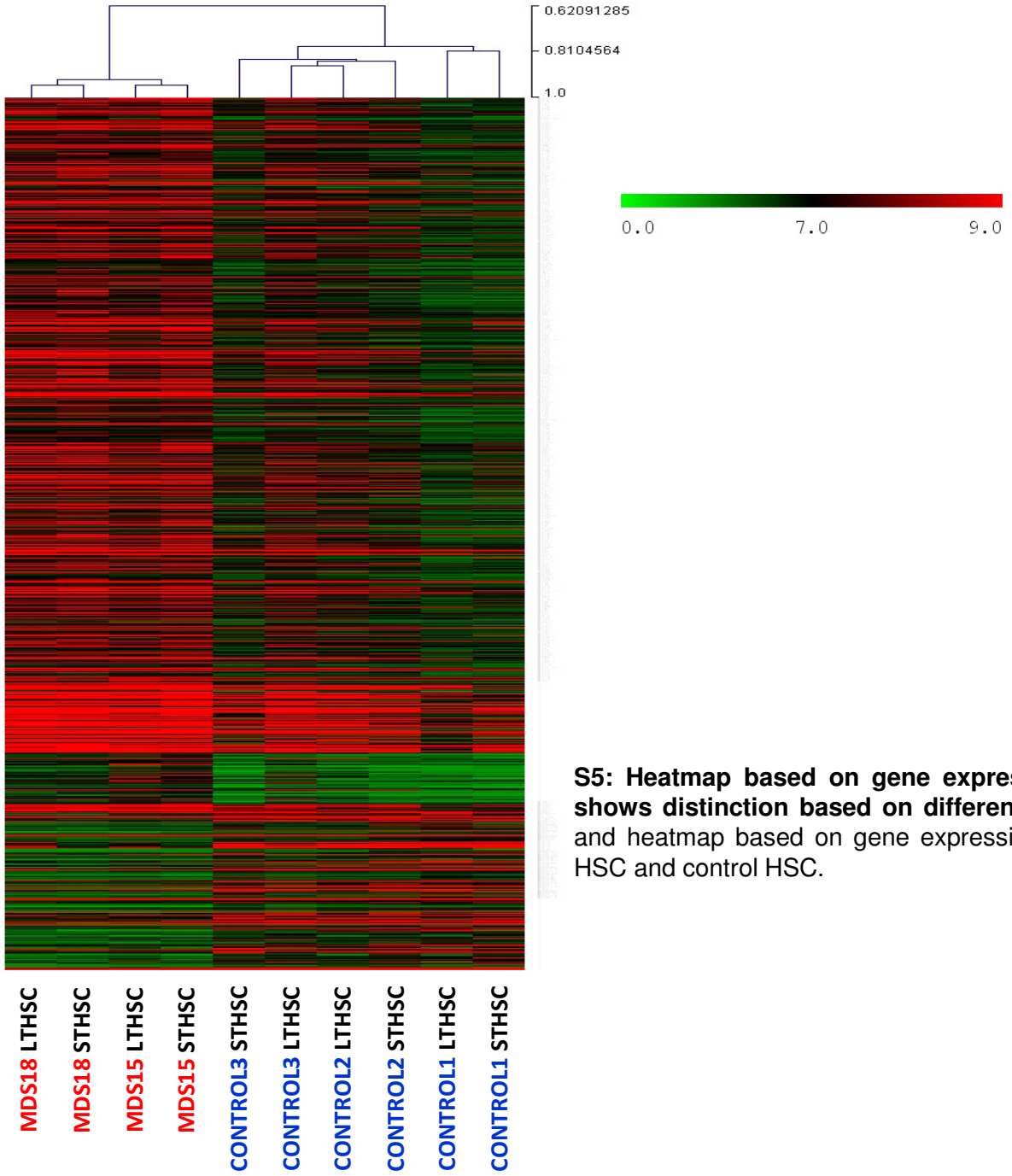

**S3: Unsupervised hierarchical clustering based on methylation profiled shows distinction between MDS and control HSC.** Unsupervised hierarchal clustering based on methylation data obtained from the HELP assay reveals differences between MDS and control HSC.

**Supp Fig 4**




**S4: Massarray validation of HELP assay methylation.** Methylation values obtained from the HELP assay (represented as log(HpaII/MspI)) correlate with the quantitative methylation values observed from bisulfite MassArray for multiple loci.

# Supp Fig 5




**S5: Heatmap based on gene expression profiles from MDS and Control HSC shows distinction based on differentially expressed genes.** Hierarchal clustering and heatmap based on gene expression profiling reveals differences between MDS HSC and control HSC.