Che-1/AATF promotes multiple myeloma proliferation through the maintenance of open chromatin structure.

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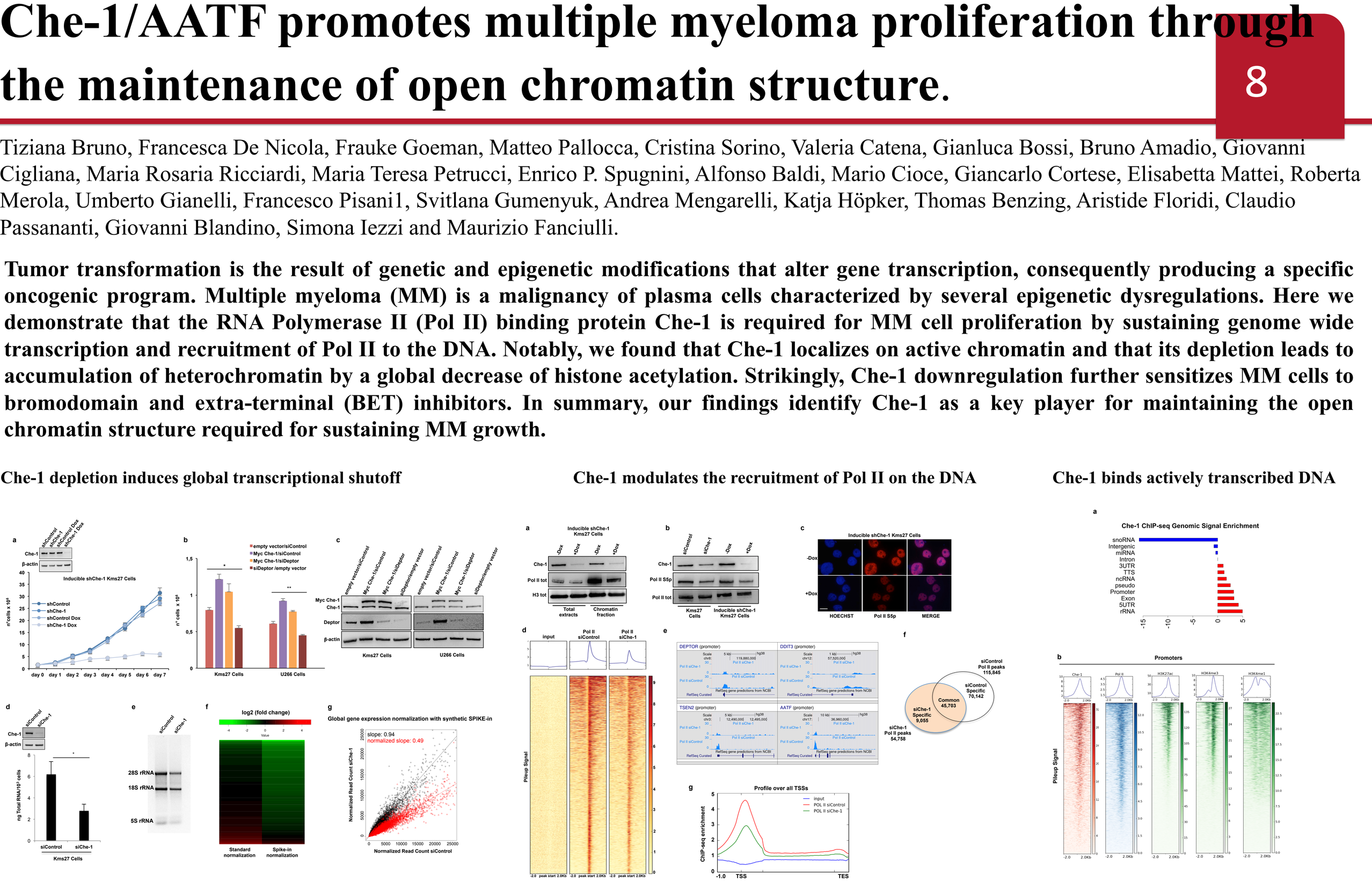
Tumor transformation is the result of genetic and epigenetic modifications that alter gene transcription, consequently producing a specific oncogenic program. Multiple myeloma (MM) is a malignancy of plasma cells characterized by several epigenetic dysregulations. Here we demonstrate that the RNA Polymerase II (Pol II) binding protein Che-1 is required for MM cell proliferation by sustaining genome wide transcription and recruitment of Pol II to the DNA. Notably, we found that Che-1 localizes on active chromatin and that its depletion leads to accumulation of heterochromatin by a global decrease of histone acetylation. Strikingly, Che-1 downregulation further sensitizes MM cells to bromodomain and extra-terminal (BET) inhibitors. In summary, our findings identify Che-1 as a key player for maintaining the open chromatin structure required for sustaining MM growth.

Che-1 depletion induces global transcriptional shutoff

Che-1 modulates the recruitment of Pol II on the DNA

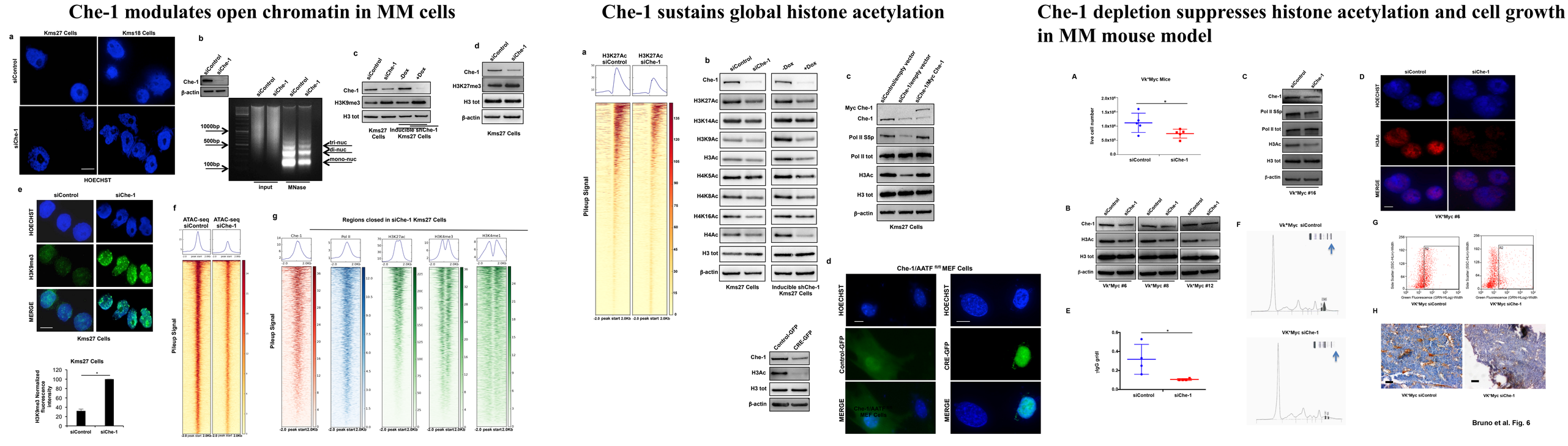
Che-1 binds actively transcribed DNA



Che-1 modulates open chromatin in MM cells

Che-1 sustains global histone acetylation

Che-1 depletion suppresses histone acetylation and cell growth in MM mouse model



Bruno et al. Fig. 6

Che-1 drives multiple myeloma pathogenesis

Che-1 expression correlates with histone acetylation in MM patients and its depletion sensitizes MM cells to BET inhibitors

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