**DAY 1**

1. The MeDIP was performed as follows: 6ug of genomic DNA was subjected to series of three 20 pulse sonications at 20% amplitude and the fragment size verified through 2% agarose gels with approximately a 500kb size.
2. The sonicated genomic DNA was resuspended to a volume of 350 ul in TE and denatured for 10 min at 95°C and then immediately placed on ice for 5 min.
3. 100 ul of 5X IP buffer (50 mM Na-phosphate pH7, 700 mM
NaCl, 0.25% Triton X-100) was added to the sonicated and denatured DNA.
4. An overnight incubation of the DNA was performed with 5 ug of antibody anti-5-methylCytidine monoclonal from Diagenode S.A at 4°C on a rotating platform.

**DAY 2**

1. Protein A/G beads from Santa Cruz were prewashed on PBS-BSA 0.1% and
resuspended in 40 ul 1X IP buffer.
2. Beads were then added to the DNA-antibody complex and incubated 2h at 4°C on a rotating platform.
3. Beads bound to DNA-antibody complex were washed 3 times with
1 ml 1X IP buffer; washes included incubation for 5min at 4°C
on a rotating platform and then centrifugation at 6000 rpm for 2 min.
4. Beads-DNA-antibodycomplex were then resuspended in 250 ul digestion buffer (50 mM Tris HCl pH 8, 10 mM EDTA, 0.5% SDS) and 3.5 ul of proteinase-k (20 mg/ml) was added to each sample and then incubated overnight at 55°C on a rotating platform.

**DAY 3**

1. DNA purification was performed first with phenol and then with chloroform:isoamyl alcohol.
2. Two washes were then performed with 70% ethanol, 1 M NaCl and glycogen.
3. ChIP selected DNA was then resuspended in 30 ul TE buffer. In order to account for ChIP bias that would interfere with the comparative hybridization, and to homogenize intra- sample variability, several parallel immunoprecipitations (IPs) were performed for each sample and then 8 successful IPs were pooled per sample; therefore one pool of IP material was made per sample or pooled group of samples.