Figure S1. Two-step mapping process employed by MethFlow in order to i) exploit the advantages of the new genome assembly models (ref. 47) and ii) recover the useful information of multiple-mapped reads for the analysis. First, the reads are mapped against a decoy assembly (canonical, alternative loci and decoy sequences). Second, some multiple-mapped reads are recovered in a second mapping step against the canonical chromosomes.
Table S1. Information stored in *NGSmethDB* for each differential methylated cytosine (DMC). All fields are described as shown in the results of *NGSmethDB API client*. Each row corresponds to a DMC, a pair of samples where it is differentially methylated and the method by which the DMC was detected and each column corresponds to a field. For more information, see the manual of *NGSmethDB*.

<table>
<thead>
<tr>
<th>Field</th>
<th>Description</th>
<th>Example</th>
</tr>
</thead>
<tbody>
<tr>
<td>chrom</td>
<td>Chromosome</td>
<td>chr22</td>
</tr>
<tr>
<td>pos</td>
<td>Chromosome position</td>
<td>25170879</td>
</tr>
<tr>
<td>methContext</td>
<td>Methylation context where is the DMC</td>
<td>CG</td>
</tr>
<tr>
<td>sample1</td>
<td>One of the two samples compared (include the name of the individual to which the sample belongs)</td>
<td>STL003.adrenalGland</td>
</tr>
<tr>
<td>sample2</td>
<td>The other of the two samples compared (include the name of the individual to which the sample belongs)</td>
<td>STL003.sigmoidColon</td>
</tr>
<tr>
<td>method</td>
<td>Method by which the DMC was detected</td>
<td>methylKit</td>
</tr>
<tr>
<td>pValue</td>
<td>p-value calculated by this method</td>
<td>0.007</td>
</tr>
<tr>
<td>consensus</td>
<td>Indicates whether it is a consensus DMC</td>
<td>True</td>
</tr>
</tbody>
</table>

Table S2. Information stored in *NGSmethDB* for each methylation segment. All fields are described as shown in the results of *NGSmethDB API client*. Each row corresponds to a methylation segment and the sample where it was detected and each column to a field. For more information, see the manual of *NGSmethDB*.

<table>
<thead>
<tr>
<th>Field</th>
<th>Description</th>
<th>Example</th>
</tr>
</thead>
<tbody>
<tr>
<td>chrom</td>
<td>Chromosome</td>
<td>chr22</td>
</tr>
<tr>
<td>start</td>
<td>Chromosome start position</td>
<td>25115312</td>
</tr>
<tr>
<td>end</td>
<td>Chromosome end position</td>
<td>25279035</td>
</tr>
<tr>
<td>methContext</td>
<td>Methylation context of the segment</td>
<td>CG</td>
</tr>
<tr>
<td>sampleCount</td>
<td>Number of samples in which this segment was detected (usually 1)</td>
<td>1</td>
</tr>
<tr>
<td>sample</td>
<td>Sample where this segment was detected</td>
<td>STL003.heartAorta</td>
</tr>
<tr>
<td>sample.methRatio</td>
<td>Average methylated reads ratio of all cytosines (in the methylation context indicated) of the segment</td>
<td>0.795</td>
</tr>
<tr>
<td>sample.cytosineCount</td>
<td>Number of cytosines (in the methylation context indicated) of the segment</td>
<td>2270</td>
</tr>
</tbody>
</table>