Appendix S1: Illustration of methods

- There are two groups in this analysis: group 1 (discovery group) and group 2 (replication group).
- Both groups contain 16 DNA samples, from 8 individuals, providing 8 genomic DNA and 8 cell line DNA samples. There is a gDNA and a clDNA sample per participant.
- Participants with T1DKD are represented by a blue circle, those with T1D and no evidence of kidney disease are represented by a green circle – this disease phenotype information is only to ensure both groups are matched for age, sex, and phenotype.
- In the diagram below, the four participants with T1DKD in group 1 are matched to the four participants with T1DKD in group 2.
- The same setup is applied for the four participants with T1D only.

![Diagram showing two groups with T1DKD and T1D participants, matched for gDNA and clDNA samples.](image)
- **Analysis 1a**: Assess differentially methylated CpG sites (dmCpGs) between gDNA and clDNA for group 1. The disease phenotypes are not under investigation.
  
  - Compare the methylation signatures for all 8 gDNA samples to all 8 clDNA samples
  - Number of differentially methylated CpG sites determined

  ![Diagram](cmpl.png)

- **Analysis 1b**: Assess dmCpGs between gDNA and clDNA for group 2.
  
  - Compare the methylation signatures for all 8 gDNA samples to all 8 clDNA samples
  - Number of differentially methylated CpG sites determined

  ![Diagram](cmpl.png)

- **Analysis 1c**: Assess overlapping dmCpGs between gDNA and clDNA.

- **Analysis 1d**: Determine the CpG sites unique to the comparison of groups 1 and 2.
- **Analysis 2**: Assess dmCpGs between gDNA and cDNA for all samples. The disease phenotypes are not under investigation.
  
  - The methylation status was quantitatively determined between the two sample types
  - The gDNA (n=16) samples originally from groups 1 and 2 were directly compared to the equivalent cDNA samples (n=16), again from groups 1 and 2
• **Analysis 3**: Assessment of differential methylation between sample groups of the same origin
  
  - The methylation status was quantitatively determined between the two sample types within groups 1 and 2
  - The gDNA (n=8) samples from group 1 were directly compared to the gDNA samples (n=8) from group 2
  - This was then repeated for the cIDNA (n=8 vs. n=8) samples