Epigenetic Methylation Study (EpiTwin)

Epigenetic Methylation Study (EpiTwin)- Plan

* European Research Council Grant

* BGi joining us

* 5 years (started in June 2010)

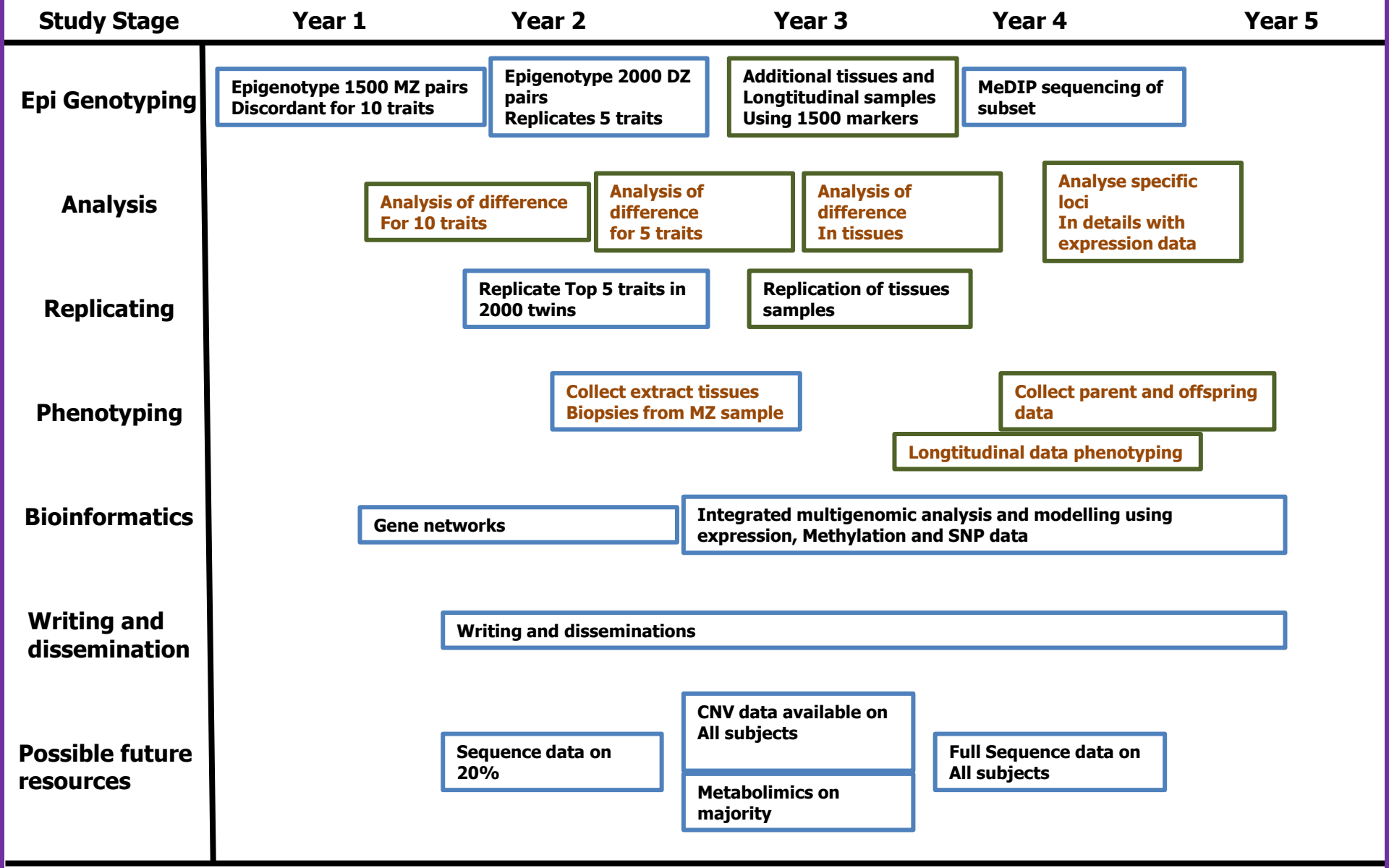
* Using already collated Phenotypic data and DNA samples from 5,000 twin pairs (3,000 MZ's and 2,000 DZ's)

* Look at epigenetic changes and how they affect 10 traits:

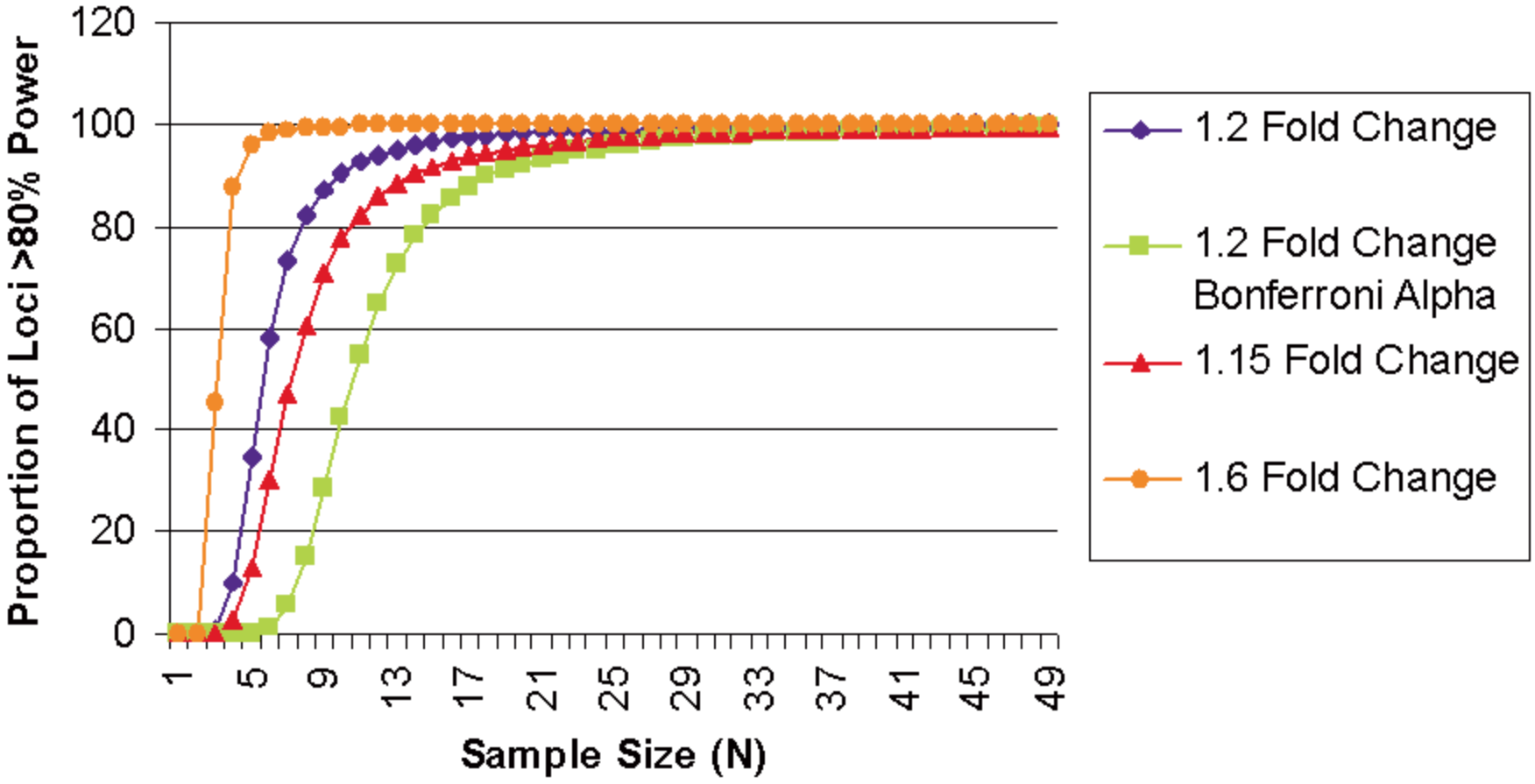
BMI	Allergy
Lipids	Lung Function
Insulin Sensitivity	Smoking
Hypertension	Platelet Volume
Bone Mineral Density	Telomere length – biochemical marker of aging

* Initial selection stage

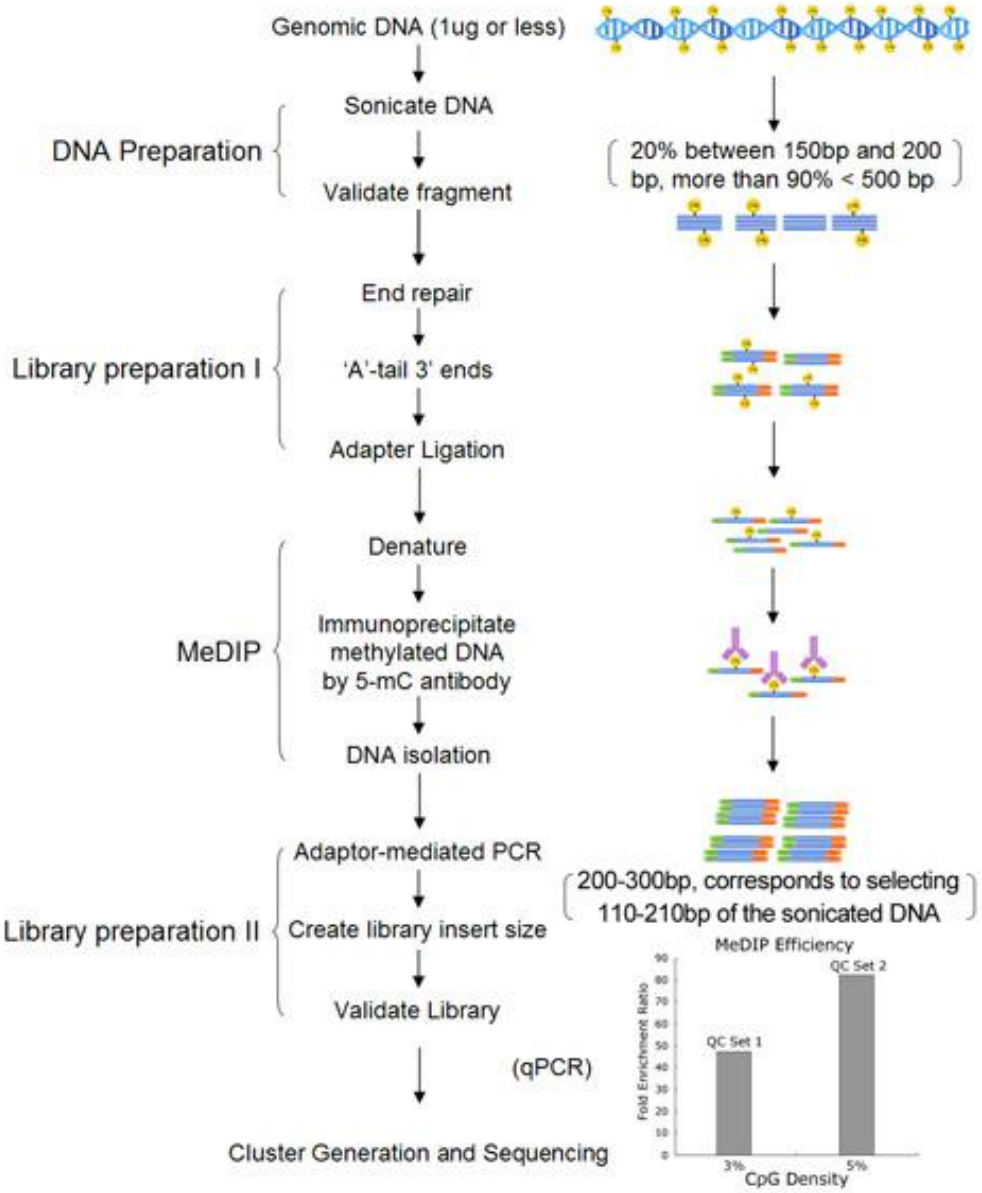
EpiTwin time line



EpiTwin's Power

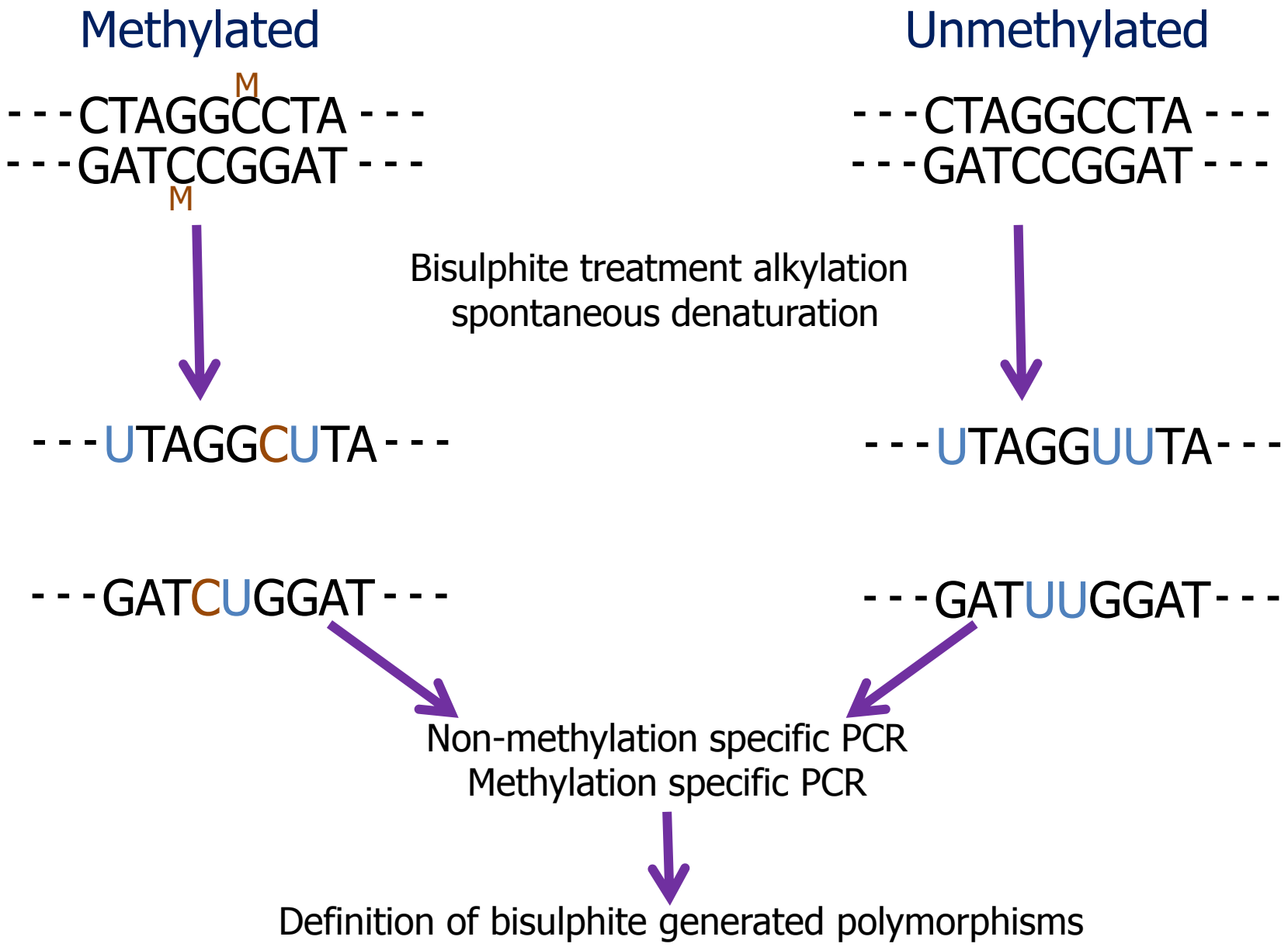


Methylated DNA immunoprecipitation Sequencing (MeDIP-sequencing)



http://www.arraystar.com/Sequencing/product_main.asp?id=206

Bisulphite Sequencing



Epigenetic changes over time

* Most epigenetic changes occur *in-utero* and within childhood

* What happens as an adult?

* Epigenetic changes are thought to take ~ 5 years

* MeDIP is currently being done on

  85 MZ pairs

  107 DZ pairs

  DNA from visit dates at least 5 years apart

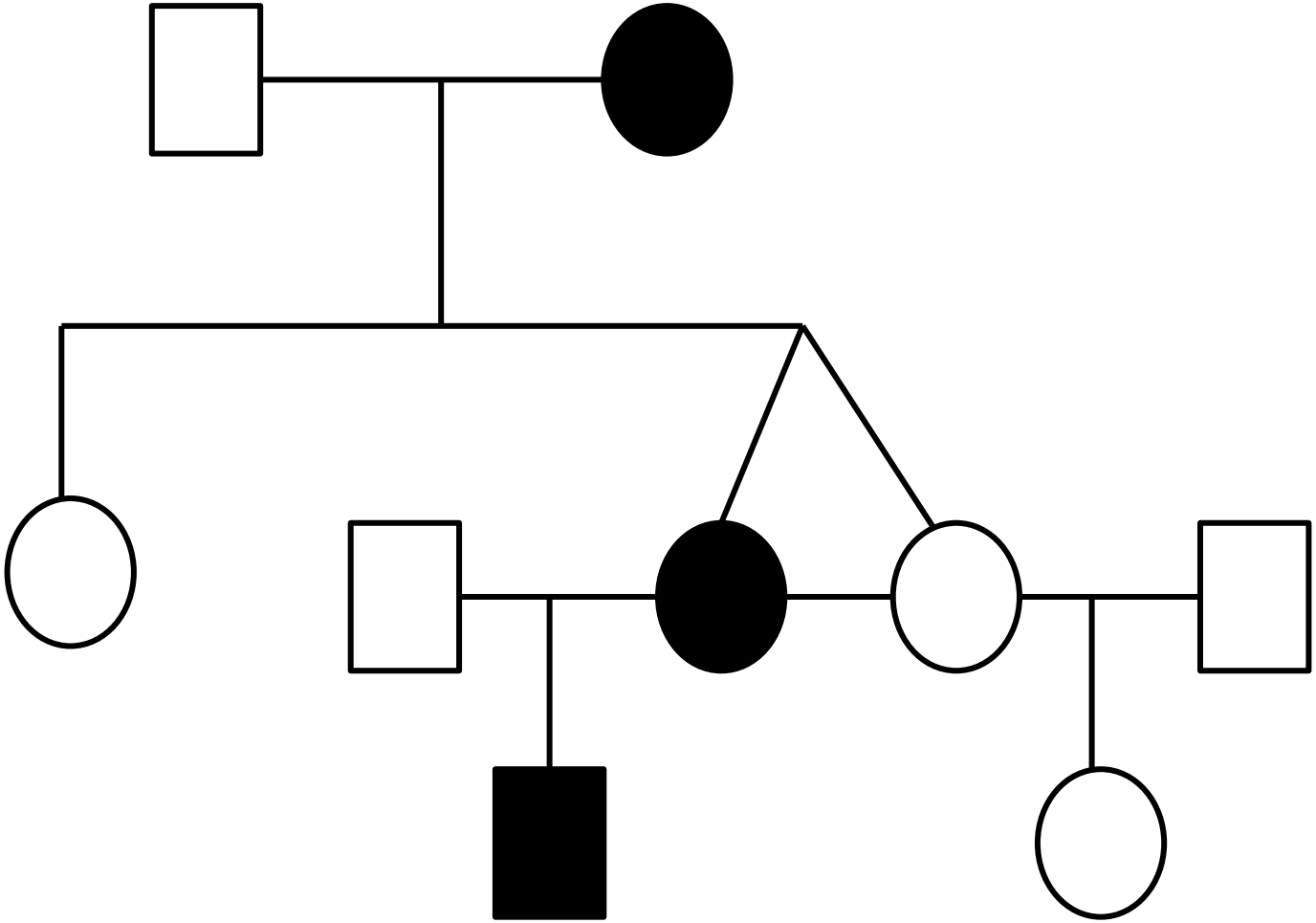
Discordant Twin Pairs

* Concentrating on MZ pairs

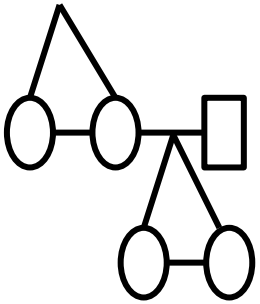
* Discordant for :
  - Type 2 Diabetes
  - Depression (Collaboration)
  - Primary Ovarian Failure (Collaboration)
  - Coronary Artery Disease (Collaboration)

* Epigenetic changes may help to determine the susceptibility of developing a disease or not

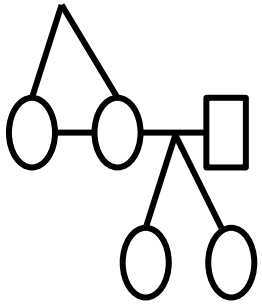
Transgenerational heritability of epigenetics – diluted over generations?



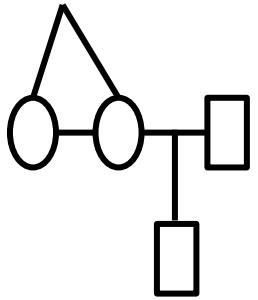
Epigenetics, transgenerational heritability – random or selected



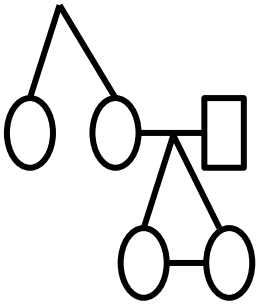
MZ offspring of MZ twin



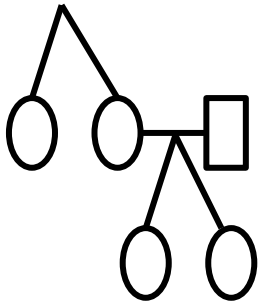
DZ offspring of MZ twin



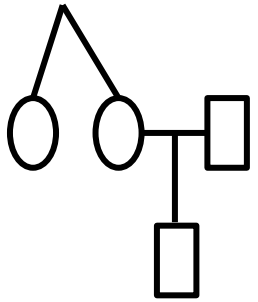
Singleton offspring of MZ twin



MZ offspring of DZ twin

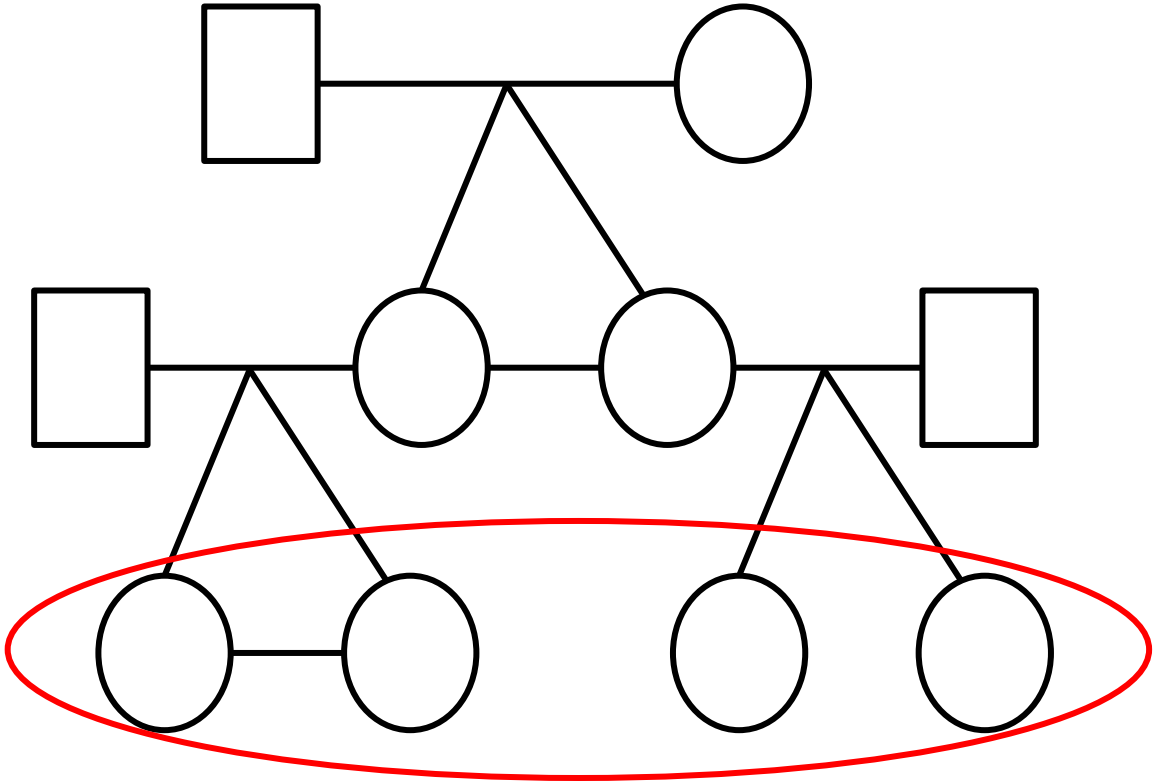


DZ offspring of DZ twin

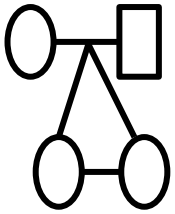


Singleton offspring of MZ twin

Epigenetics, transgenerational heritability – within generations



Epigenetics – early epigenetics



MZ twins

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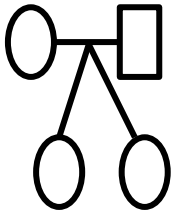
Shared genetics
Shared inter-uterine environment
Shared early childhood



DZ twins

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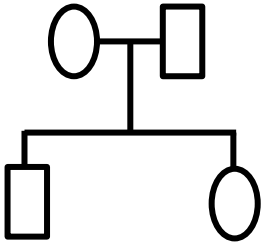
Different genetics
Shared inter-uterine environment
Shared early childhood



Singleton offspring

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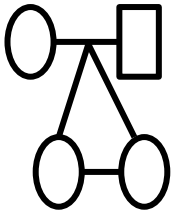
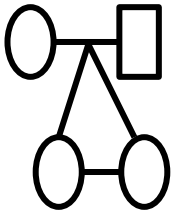
Different genetics
Different inter-uterine environment
Shared early childhood

EpiTwin – potential models

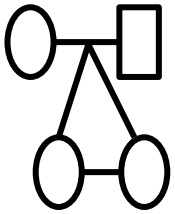
Epigenetics – early environment



MZ twins → Reared together

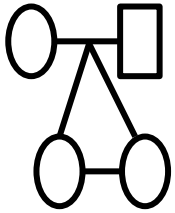


MZ twins → Adopted and reared together

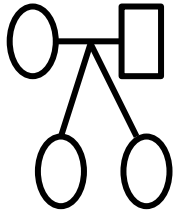


MZ twins → Adopted and reared apart

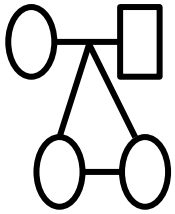
Epigenetics – early environment



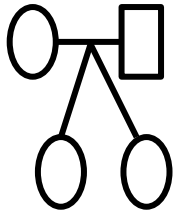
MZ twins → Naturally conceived



DZ twins → Naturally conceived

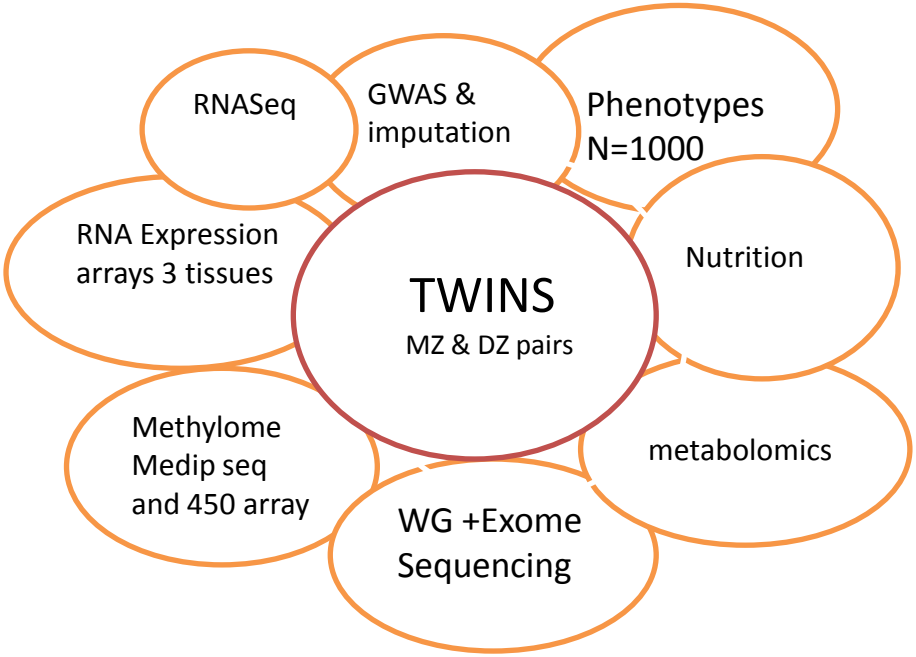


MZ twins → IVF



DZ twins → IVF

TwinsUK + MuTHER – A complete omic resource



Acknowledgments

华大基因

BGI