Identical twins carry a persistent epigenetic signature of early genome programming.

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Monozygotic (MZ) twins and higher-order multiples arise when a zygote splits during pre-implantation stages of development. The mechanisms underpinning this event have remained a mystery. Because MZ twinning rarely runs in families, the leading hypothesis is that it occurs at random. Here, we show that MZ twinning is strongly associated with a stable DNA methylation signature in adult somatic tissues. This signature spans regions near telomeres and centromeres, Polycomb-repressed regions and heterochromatin, genes involved in cell-adhesion, WNT signaling, cell fate, and putative human metastable epialleles. Our study also demonstrates a never-anticipated corollary: because identical twins keep a lifelong molecular signature, we can retrospectively diagnose if a person was conceived as monozygotic twin.

I gemelli monozigoti(MZ) o multipli superiori monozigoti si verificano quando uno zigote si divide nella fase pre-impianto. Il meccanismo attraverso il quale questo avviene rimane un mistero. E' raro che i gemelli monozigoti si verifichino nelle famiglie e quindi l'evento viene ritenuto "casuale".In questo lavoro mostriamo che il gemellaggio monozigote si associa con una "firma" epigenetica di metilazione del DNA stabile nei tessuti somatici adulti.
Questa marcatura si trova in regioni vicino a telomeri e centromeri , regioni represse da Polycomd ed eterocromatina, geni coinvolti nella adesione cellulare , segnalazione WNT, cellule e epialleli metastabili umani putativi. Il nostro studio dimostra anche un corollario mai anticipato:
poiché i gemelli identici mantengono una firma molecolare per tutta la vita, possiamo diagnosticare retrospettivamente se una persona sia stata concepita come gemello monozigote.

Il lavoro presentato eseguito su gemelli monozigoti con gruppo controllo di gemelli dizigoti ha avuto come obiettivo quello di fare luce circa le segnature epigenetiche presenti nei gemelli monozigoti. La gemellarità monozigotica avviene casualmente non essendo nota dinamica famigliare. Le gravidanze gemellari monozigotiche hanno un rischio aumentato di complicanze ostetriche perinatali e neonatali. La gemellarità monozigotica colpisce circa il 12% delle gravidanze ma poi giunge al termine con un parto gemellare solo al 2% per riassorbimento di uno dei due gemelli e si produce all'inizio della gestazione, nella fase zigotica, quando prende piede la maggiore ri-programmazione epigenetica. Molto presto dopo il concepimento il metiloma dell'embrione va incontro ad una ondata di globale demetilazione seguita da metilazione de novo. La metilazione avviene per dar modo alle cellule totipotenti di trasformarsi nelle varie linee di differenziazione ed è essenziale er lo sviluppo embrionale. Il lavoro mostra che il gemellaggio monozigote è associato a un profilo di metilazione del DNA persistente nei tessuti somatici dei soggetti adulti.
La firma del gemellaggio monozigote comprende 834 siti CpG , geni coinvolti nella adesione cellulare, segnalazione nella via WNT e destino cellulare. Le marcature sono più presenti vicino ai telomeri e ai centromeri. Il gemellaggio monozigote dunque ha una forte firma epigenetica (nei campioni di gemelli monozigoti le marcature degli 834 siti CpG sono in media quasi tre volte più grandi che nei campioni dizigoti). Le marcature sono fortemente condizionate dalla genetica cn interazioni alleliche o gene-gene. Le marcature con il lavoro messe in evidenza sono stabili nelle cellule somatiche e dunque è possibile risalire alla presenza di una gemellarità
nelle primissime epoche della vita fetale anche quando non sia noto in vita adulta (per riassorbimento dell'embrione gemello all'inizio della gravidanza).

Genetic and environmental factors of schizophrenia and autism spectrum disorder: insights from twin studies

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Twin studies of psychiatric disorders such as schizophrenia and autism spectrum disorder have employed epidemiological approaches that determine heritability by comparing the concordance rate between monozygotic twins (MZs) and dizygotic twins. The basis for these studies is that MZs share 100% of their genetic information. Recently, biological studies based on molecular methods are now being increasingly applied to examine the differences between MZs discordance for psychiatric disorders to unravel their possible causes. Although recent advances in next-generation sequencing have increased the accuracy of this line of research, there has been greater emphasis placed on epigenetic changes versus DNA sequence changes as the probable cause of discordant psychiatric disorders in MZs. Since the epigenetic status differs in each tissue type, in addition to the DNA from the peripheral blood, studies using DNA from nerve cells induced from postmortem brains or induced pluripotent stem cells are being carried out. Although it was originally thought that epigenetic changes occurred as a result of environmental factors, and thus were not transmittable, it is now known that such changes might possibly be transmitted between generations. Therefore, the potential possible effects of intestinal flora inside the body are currently being investigated as a cause of discordance in MZs. As a result, twin studies of psychiatric disorders are greatly contributing to the elucidation of genetic and environmental factors in the etiology of psychiatric conditions.

Relationship between Nutrient Intake and Human Gut Microbiota in Monozygotic Twins

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The gut microbiota is associated with human health and dietary nutrition. Various studies have been reported in this regard, but it is difficult to clearly analyze human gut microbiota as individual differences are significant. The causes of these individual differences in intestinal microflora are genetic and/or environmental. In this study, we focused on differences between identical twins in Japan to clarify the effects of nutrients consumed on the entire gut microbiome, while excluding genetic differences. *Materials and Methods*: We selected healthy Japanese monozygotic twins for the study and confirmed their zygosity by matching 15 short tandem repeat loci. Their fecal samples were subjected to 16S rRNA sequencing and bioinformatics analyses to identify and compare the fluctuations in intestinal bacteria. *Results*: We identified 12 genera sensitive to environmental factors, and found that *Lactobacillus* was relatively unaffected by environmental factors. Moreover, we identified protein, fat, and some nutrient intake that can affect 12 genera, which have been identified to be more sensitive to environmental factors. Among the 12 genera, *Bacteroides* had a positive correlation with retinol equivalent intake (*rs* = 0.38), *Lachnospira* had a significantly negative correlation with protein, sodium, iron, vitamin D, vitamin B6, and vitamin B12 intake (*rs* = -0.38, -0.41, -0.39, -0.63, -0.42, -0.49, respectively), *Lachnospiraceae* ND3007 group had a positive correlation with fat intake (*rs* = 0.39), and *Lachnospiraceae* UCG-008 group had a negative correlation with the saturated fatty acid intake (*rs* = -0.45). *Conclusions*: Our study is the first to focus on the relationship between human gut microbiota and nutrient intake using samples from Japanese twins to exclude the effects of genetic factors. These findings will broaden our understanding of the more intuitive relationship between nutrient intake and the gut microbiota and can be a useful basis for finding useful biomarkers that contribute to human health.