Unlocking Personalised Medicine in Obesity

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More than 1 billion people worldwide have obesity, including 150 million children. Obesity is a complex, multifactorial condition with a strong genetic basis, encompassing both monogenic, oligogenic and polygenic contributions. Since the discovery of leptin, more than 85 forms of monogenic conditions have been identified, where early-onset obesity with impaired appetite regulation is the prominent phenotype, but usually associated with neuro developmental (and other) phenotypes which makes monogenic obesity mostly syndromic. Genome-wide association studies (GWAS) have identified over 1,000 loci associated with weight variation and with common forms of obesity. Most of these genes are expressed in the brain, and many are related to the reward and addiction circuities. While polygenic risk scores can predict risk (or protection) for incident obesity, lifestyle factors such as physical activity can partly mitigate this risk. A continuum exists between monogenic and polygenic obesity, likely including intermediate oligogenic forms. Innovative therapies, such as melanocortin 4 receptor (MC4R) agonists, and the incretins-receptors agonists that are anti-addictive drugs, are paving the way for precision medicine approaches. These advancements offer new opportunities to tailor prevention and treatments to the underlying genetic causes of obesity. Therefore, unlocking real-world personalized prevention and care of obesity and co-morbidities is both an opportunity and a challenge of these times.