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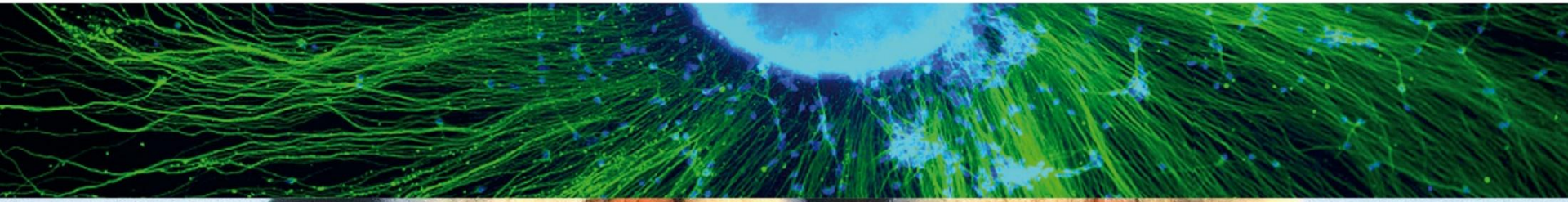

ESF-EMRC Science Policy Briefing
Open Access in Biomedical Research
Consejo Superior de Investigaciones Científicas (CSIC)
Madrid, Spain, 21 March 2012

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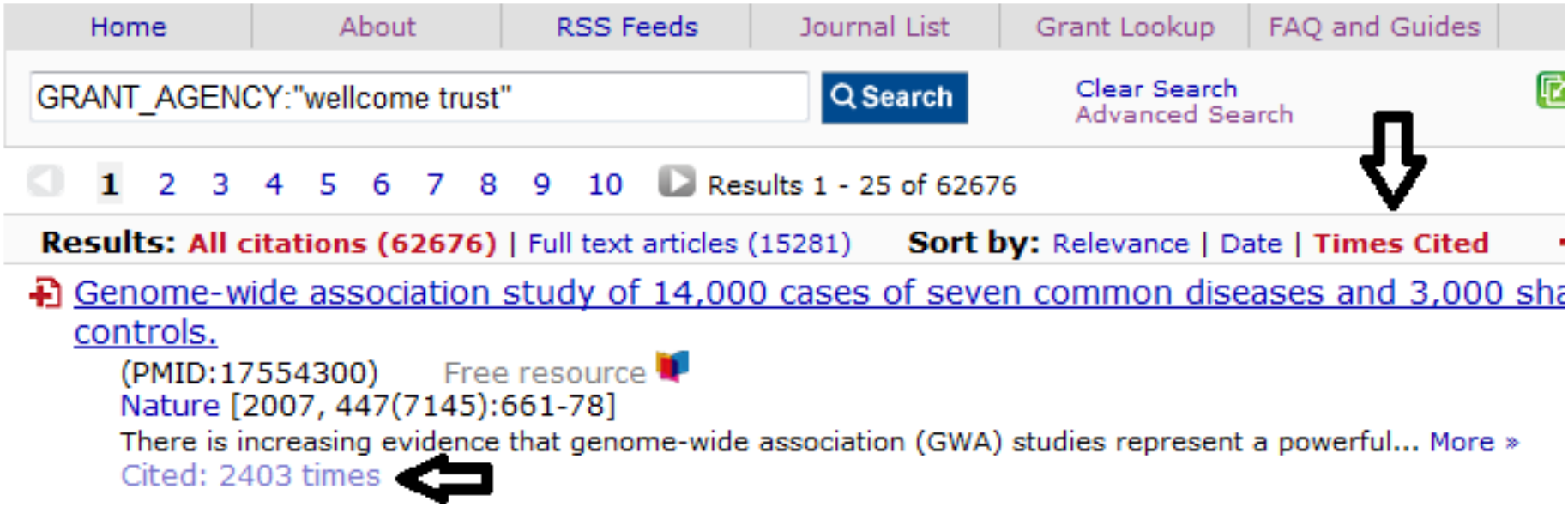
UK and UKPMC

- UK main biomedical research funders have implemented similar open access policies and a unique repository – UKPMC
- Hosted by European Bioinformatics Institute
- 16 funders, including 2 European – 2nd round of funding for 5 years
- Part of the PMCI programme and built in collaboration with NCBI
- Mirror of PubMed and PMC, with additional resources (Agricola, European Patent Office)
- Mix of Green, Hybrid and Gold open access, with some publishers only allowing depositing if Author fee is paid
- UKPMC+ - grant reporting tool – enable to associate funding with publication
- Citation information integrated

Europe PMC – benefits

- Increase visibility and accessibility of research results – through PubMed and Google Scholar
- One-stop search functionality, including link to databases (genes, proteins, etc)
- Citation information for researchers, including Scopus and Web of Science
- Standard format (XML) of paper enable text mining, and easy information exchange
- Pooling resources together – state of the art system at a reasonable cost.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Genome-wide association study of 14,000 cases of seven common diseases and 3,000 sha
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(PMID:17554300)
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Nature [2007, 447(7145):661-78]
There is increasing evidence that genome-wide association (GWA) studies represent a powerful... More »
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Common variants near MC4R are associated with fat mass, weight and risk of obesity.

(PMID:18454148)

Abstract | Citations | BioEntities | Related Articles

Loos RJ, Lindgren CM, Li S, Wheeler E, Zhao JH, Prokopenko I, Inouye M, Freathy RM, Attwood AP, Beckmann JS, Berndt SI, Prostate, Lung, Colorectal, and Ovarian (PLCO) Cancer Screening Trial, Jacobs KB, Chanock SJ, Hayes RB, Bergmann S, Bennett AJ, Bingham SA, Bochud M, Brown M, Cauchi S, Connell JM, Cooper C, Smith GD, Day I, Dina C, De S, Dermitzakis ET, Doney AS, Elliott KS, Elliott P, Evans DM, Sadaf Farooqi I, Froguel P, Ghori J, Groves CJ, Gwilliam R, Hadley D, Hall AS, Hattersley AT, Hebebrand J, Heid IM, KORA, Lamina C, Gieger C, Illig T, Meitinger T, Wichmann HE, Herrera B, Hinney A, Hunt SE, Jarvelin MR, Johnson T, Jolley JD, Karpe F, Keniry A, Khaw KT, Luben RN, Mangino M, Marchini J, McArdle WL, McGinnis R, Meyre D, Munroe PB, Morris AD, Ness AR, Neville MJ, Nica AC, Ong KK, O'Rahilly S, Owen KR, Palmer CN, Papadakis K, Potter S, Pouta A, Qi L, Nurses' Health Study, Randall JC, Rayner NW, Ring SM, Sandhu MS, Scherag A, Sims MA, Song K, Soranzo N, Speliotes EK, Diabetes Genetics Initiative, Syddall HE, Teichmann SA, Timpson NJ, Tobias JH, Uda M, SardiNIA Study, Vogel CI, Wallace C, Waterworth DM, Weedon MN, Wellcome Trust Case Control Consortium, Willer CJ, FUSION, Wraight, Yuan X, Zeggini E, Hirschhorn JN, Strachan DP, Ouwehand WH, Caulfield MJ, Samani NJ, Frayling TM, Vollenweider P, Waeber G, Mooser V, Deloukas P, McCarthy MI, Wareham NJ, Barroso I, Jacobs KB, Chanock SJ, Hayes RB, Lamina C, Gieger C, Illig T, Meitinger T, Wichmann HE, Kraft P, Hankinson SE, Hunter DJ, Hu FB, Lyon HN, Voight BF, Ridderstrale M, Groop L, Scheet P, Sanna S, Abecasis GR, Albai G, Nagaraja R, Schlessinger D, Jackson AU, Tuomilehto J, Collins FS, Boehnke M, Mohlke KL

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Nature Genetics [2008, 40(6):768-75]

Type: Journal Article, Multicenter Study, Research Support, Non-U.S. Gov't, Research Support, N.I.H., Extramural

DOI: 10.1038/ng.140

Abstract

Highlight Terms

Diseases(2) Genes/Proteins(2)

To identify common variants influencing body mass index (BMI), we analyzed genome-wide association data from 16,876 individuals of European descent. After previously reported variants in FTO, the strongest association signal (rs17782313, P = 2.9 x 10(-6)) mapped 188 kb downstream of MC4R (melanocortin-4 receptor), mutations of which are the leading cause of monogenic severe childhood-onset obesity. We confirmed the BMI association in 60,352 adults (per-allele effect = 0.05 Z-score units; P = 2.8 x 10(-15)) and 5,988 children aged 7-11 (0.13 Z-score units; P = 1.5 x 10(-8)). In case-control analyses (n = 10,583), the odds for severe childhood obesity reached 1.30 (P = 8.0 x 10(-11)). Furthermore, we observed overtransmission of the risk allele to obese offspring in 660 families (P (pedigree disequilibrium test average; PDT-avg) = 2.4 x 10(-4)). The SNP location and patterns of phenotypic associations are consistent with effects mediated through altered MC4R function. Our findings establish that common variants near MC4R influence fat mass, weight and obesity risk at the population level and reinforce the need for large-scale data integration to identify variants influencing continuous biomedical traits.

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Obesity
Polymorphism, Single Nucleotide
Proteins
Quantitative Trait Loci
Randomized Controlled Trials as Topic
Receptor, Melanocortin, Type 4

units, $P = 3.0 \times 10^{-5}$; Fig. 3 and Supplementary Table 5).

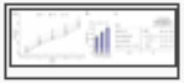

Figure 3
Effects of rs17782313 on regulation of weight in early life. (**a**) Longitudinal data for BMI at age 7–11 for children in the ALSPAC study by rs17782313 genotypes. Mean values represented as geometric means and back-transformed 95% confidence intervals. (more ...)

These findings were confirmed in three case-control studies of children and adolescents with severe early-onset obesity (Supplementary Note, Supplementary Fig. 1 and Supplementary Table 1). In each, rs17782313 was associated with a significant increase in the risk of extreme obesity: the combined estimate of the OR was 1.30 (1.20–1.41; $P = 8.0 \times 10^{-11}$; Fig. 3 and Supplementary Table 1). In 660 nuclear families, ascertained through children or adolescents with extreme obesity (BMI > 95th percentile), there was a significant overtransmission of the C allele to the obese offspring (56% transmission rate, PDT-avg = 2.42×10^{-4}), providing further evidence that the association does not reflect population stratification (Supplementary Note, Supplementary Fig. 1 and Supplementary Table 1).

Common variants near *MC4R* and *FTO* seem to have additive effects on BMI (Fig. 4). When comparing individuals with no risk alleles at either locus (19% of the population) with those homozygous at both (1%), the point estimate of the BMI difference amounts to 0.26 *Z*-score units (or ~1.17 kg m^{-2}) in adults and 0.56 *Z*-score units in children.

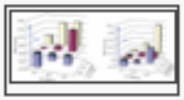

Figure 4
Association between the combined rs17782313 and *FTO* genotypes and BMI in adults (EPIC-Norfolk, n = 15,622) and children (ALSPAC age 7 years, n = 5,779). BMI is expressed in $\log_{10}$BMI *Z*-score units adjusted for age (in adults) and sex. Both SNPs have a (more ...)

Having observed convincing BMI and obesity associations in both adults and children, we next sought refinement of the association signal through meta-analyses of genotyped and imputed data and analysis of LD patterns (Supplementary Fig. 5a online) across 1 Mb of flanking sequence (including the coding region of *MC4R* itself). In contrast to the original analysis of all seven studies (Fig. 1), the meta-analysis restricted to the four population-based studies (Supplementary Fig. 5b)

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Europe PMC – challenges

- Technical
  - few as infrastructure is in place / need to develop interoperability
- Legal and governance
  - collaborative model
- Financial
  - proportionate to size of funding budget
- Policy
  - need for consistency

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