Association of maternal G protein β3 subunit 825T allele with low birthweight

Berthold Hocher, Torsten Slowinski, Thomas Stolze, Aiko Pleschka, Hans-H Neumayer, Horst Halle

See Commentary page 1201

Weight at birth has been associated with an increased risk for cardiovascular disease and type 2 diabetes in adult life. We found an association between the maternal G protein β3 subunit 825T allele and low birthweight in babies born to women without other risks for reduced fetal growth.

Cardiovascular diseases such as hypertension, coronary-artery disease, and type 2 diabetes are inversely associated with birthweight. Apart from pregnancy-associated hypertension, proteinuria, impaired glucose tolerance, pre-eclampsia, eclampsia, haemolysis, elevated liver enzymes, and low platelet count (HELLP) syndrome, or signs of any placental abnormalities on ultrasonography. All babies were examined by the paediatric consultant. Genotyping was done in all 181 eligible women and in 113 babies, 68 mothers refused to allow blood samples taken from their babies for genotyping.

Maternal and neonate genomic DNA was prepared from peripheral white blood cells. PCR amplification was done in all 181 eligible women and in 113 babies. 68 mothers refused to allow blood samples taken from their babies for genotyping.

The maternal T allele is associated with birthweight a mean of 207 g lower than that associated with the C allele (CC mothers; 3542 [496] g, n=75; CT and TT mothers 3472 [1076] g, n=106; p<0.05).

Mothers’ and babies characteristics are given in the table. Fetal G protein β3 subunits (C825T) polymorphism did not affect birthweight. Maternal CT genotype was associated with a significantly (p=0.015) lower birthweight than the CC genotype, as was the maternal TT mean genotype (table), but not significantly so (p=0.18), probably because of the low number of TT mothers in our study. Since the cellular phenotype (increased G-protein activity) is similar in the TT and CT genotype, compared with the CC genotype, we thought it was better to analyse the CT and TT mothers together. This analysis showed that the maternal T allele is associated with birthweight a mean of 207 g lower than that associated with the C allele (CC mothers; 3542 [496] g, n=75; CT and TT mothers 3472 [1076] g, n=106; p<0.05).

Mothers’ and babies characteristics are given in the table. Fetal G protein β3 subunits (C825T) polymorphism did not affect birthweight. Maternal CT genotype was associated with a significantly (p=0.015) lower birthweight than the CC genotype, as was the maternal TT mean genotype (table), but not significantly so (p=0.18), probably because of the low number of TT mothers in our study. Since the cellular phenotype (increased G-protein activity) is similar in the TT and CT genotype, compared with the CC genotype, we thought it was better to analyse the CT and TT mothers together. This analysis showed that the maternal T allele is associated with birthweight a mean of 207 g lower than that associated with the C allele (CC mothers; 3542 [496] g, n=75; CT and TT mothers 3472 [1076] g, n=106; p<0.05).

Mothers’ and babies characteristics are given in the table. Fetal G protein β3 subunits (C825T) polymorphism did not affect birthweight. Maternal CT genotype was associated with a significantly (p=0.015) lower birthweight than the CC genotype, as was the maternal TT mean genotype (table), but not significantly so (p=0.18), probably because of the low number of TT mothers in our study. Since the cellular phenotype (increased G-protein activity) is similar in the TT and CT genotype, compared with the CC genotype, we thought it was better to analyse the CT and TT mothers together. This analysis showed that the maternal T allele is associated with birthweight a mean of 207 g lower than that associated with the C allele (CC mothers; 3542 [496] g, n=75; CT and TT mothers 3472 [1076] g, n=106; p<0.05).

Mothers’ and babies characteristics are given in the table. Fetal G protein β3 subunits (C825T) polymorphism did not affect birthweight. Maternal CT genotype was associated with a significantly (p=0.015) lower birthweight than the CC genotype, as was the maternal TT mean genotype (table), but not significantly so (p=0.18), probably because of the low number of TT mothers in our study. Since the cellular phenotype (increased G-protein activity) is similar in the TT and CT genotype, compared with the CC genotype, we thought it was better to analyse the CT and TT mothers together. This analysis showed that the maternal T allele is associated with birthweight a mean of 207 g lower than that associated with the C allele (CC mothers; 3542 [496] g, n=75; CT and TT mothers 3472 [1076] g, n=106; p<0.05).
Endosymbiotic bacteria in worms as targets for a novel chemotherapy in filariasis

Achim Hoerauf, Lars Volkmann, Christoph Hamelmann, Ohene Adjei, Ingo B Autenrieth, Bernhard Fleischer, Dietrich W Büttner

Endosymbiotic bacteria living in plasmodia or worm parasites are required for the homoeostasis of their host and should be excellent targets for chemotherapy of certain parasitic diseases. We show that targeting of Wolbachia spp bacteria in Onchocerca volvulus filariae by doxycycline leads to sterility of adult worms to an extent not seen with drugs used against onchocerciasis, a leading cause of blindness in African countries.

Filariae are responsible for devastating diseases in man, including blindness and elephantiasis, with 150 million infections worldwide. The world community had made it a goal to interrupt transmission and to eliminate these diseases.1 However, present chemotherapy such as ivermectin (drug of first choice) are mainly targeted at mature microfilariae, and not at adult worms or early embryos, leading to a reappearance of skin microfilariae several months after treatment. Since adult worms have a long lifespan (up to 15 years), mass treatment will have to be maintained for many years if transmission is to be interrupted.1 Computer simulation shows tremendous risks in these programmes with present drugs alone.2 There is thus a pressing need for new antifilarial drugs that have microfilaricidal efficacy or that show total and longlasting suppression of embryo production, to complement microfilaricides such as ivermectin.3

Evidence from work in animals shows that Wolbachia spp (order Rickettsiales) endobacteria in filariae are targets for chemotherapy, since their depletion by tetracycline led to degeneration and sterility of adult worms.4,5 This approach has not been examined in human filariasis. Therefore, we investigated the effectiveness of targeting wolbachia in human onchocerciasis with respect to worm fertility and survival.

In an area of Ghana outside the onchocerciasis control programme, volunteer onchocerciasis patients aged 18–50 years who had not had ivermectin were assigned, after informed consent, to a control group or to treatment with doxycycline (Vibramycin, Pfizer; 100 mg orally per day) for 6 weeks. Daily tablet intake was supervised. 4 months after the end of treatment, which was well tolerated in all cases, onchocercomata (nodules containing one to six female worms) were excised and coded for blinded examinations by two independent examiners. One part of each nodule was processed for semi quantitative PCR to quantify bacterial