

Obesity was associated with reduced LH pulse amplitude and a reduced LH response to 75 ng/kg GnRH; markers of hypothalamic function were not affected by BMI. The authors conclude that BMI influences LH response to GnRH at the pituitary, not hypothalamic, level, perhaps through decreased pituitary responsiveness. They suggest that affected women with high and low BMIs, respectively, do not comprise distinct patient subgroups, as suggested by some previous studies.

Original article Pagán YL *et al.* (2006) Inverse relationship between LH and BMI in PCOS: investigation of hypothalamic and pituitary contributions. *J Clin Endocrinol Metab* **91**: 1309–1316

Low-cost, rapid, and reliable screening for *MEN1* mutations

Currently, direct DNA sequencing is the method of choice for detecting mutations in *MEN1* (the gene associated with multiple endocrine neoplasia type 1). As no mutational hotspots exist in *MEN1*, the entire gene must be sequenced, which is slow, labor intensive, and expensive. Denaturing high-performance liquid chromatography (DHPLC) is successfully used in the high-throughput, automated detection of mutations in other tumor-associated genes, and researchers in France have now confirmed that DHPLC can detect *MEN1* mutations with 100% sensitivity, equivalent to the sensitivity of DNA sequencing. Crépin *et al.* retrospectively analyzed 160 samples from unrelated patients with *MEN1* for whom sequence data were available, as well as positive and negative control samples. DHPLC results were obtained within a few hours.

MEN1 mutations reveal characteristic patterns on DHPLC, which differ from those generated by wild-type DNA, but confirmatory DNA sequencing is still required to identify specific mutations. Nonetheless, because DHPLC can reliably screen out samples containing only wild-type *MEN1* and target potentially mutated DNA fragments, the authors estimate the overall cost of *MEN1* genotypic diagnosis using DHPLC to be fivefold cheaper than diagnosis based on complete DNA sequencing. Neither DNA sequencing nor DHPLC can identify deletion or duplication of entire exons, however, detection of which requires quantitative analysis techniques.

DHPLC is based on the detection of DNA heteroduplexes formed in polymerase chain reaction products. The authors highlight that the specificity of DHPLC (98.6% in this study) depends on the purity of these products.

Original article Crépin M *et al.* (2006) Evaluation of denaturing high performance liquid chromatography for the mutational analysis of the *MEN1* gene. *J Mol Endocrinol* **36**: 369–376

Could calorie restriction truly make you live longer?

Researchers are now a step closer to answering that question, following publication of a study that investigated the effects of a 6-month calorie-restricted diet on several biomarkers of metabolic adaptation and oxidative stress. Heilbronn *et al.* found that prolonged calorie restriction reduced fasting insulin levels and body temperature (both factors are associated with longevity in animal studies). Their findings support the theory that caloric restriction is associated with a greater decrease in energy expenditure than would be expected to result solely from a reduction in metabolic mass.

A particular strength of their study was that all dietary regimes were calculated individually for each participant, from measurements of baseline energy requirements. Heilbronn *et al.* randomly allocated 48 healthy, overweight men and women (BMI between 20 and 30 kg/m²) among four groups: 12 controls received a weight-maintenance diet; 12 individuals received a calorie-restricted diet of 25% below baseline requirements; 12 individuals received a 12.5% calorie-restricted diet plus an exercise regimen; and 12 individuals received a low-calorie diet (890 kcal daily) until 15% weight-loss had been achieved, followed by a maintenance diet. Importantly, individuals' metabolic adaptations to calorie restriction occurred during the first 3 months of the study, although weight loss continued. Interestingly, reduced DNA damage was observed in calorie-restricted individuals in parallel with a decline in their oxygen consumption; additional studies might clarify whether calorie restriction reduces oxidative stress, and could detect changes in other biomarkers of longevity.

Original article Heilbronn LK *et al.* (2006) Effect of 6-month calorie restriction on biomarkers of longevity, metabolic adaptation, and oxidative stress in overweight individuals: a randomized controlled trial. *JAMA* **295**: 1539–1548