it has a folk medicine history as an anticonvulsant. Now recent research explains why it’s been used to combat some seizures.

In a recent FASEB Journal study, researchers at the University of California, Irvine (UCI), reported that cilantro, or Coriandrum sativum, is a potent activator of neuronal voltage-gated potassium channel subfamily Q (KCNQ). Mutations in most of the genes that express this family of potassium channels can lead to heart disease, deafness, and severe epilepsy syndromes that are resistant to modern anticonvulsants.

By screening cilantro leaf metabolites, the researchers found that one—the long-chain fatty aldehyde (E)-2-dodecenal—activates several KCNQ channels, including the predominant neuronal and cardiac isoforms that regulate electrical activity in the brain and heart. “[D]odecenal binds to a specific part of the potassium channels to open them, reducing cellular excitability” and seizure activity, Geoff Abbott, PhD, professor of physiology and biophysics at the UCI School of Medicine, said in a statement. The metabolite also delayed some tonic seizures in mice.

Abbott said the finding “is important, as it may lead to more effective use of cilantro as an anticonvulsant or to modifications of dodecenal to develop safer and more effective anticonvulsant drugs.”

**Do Mushrooms Really Protect Against Cardiometabolic Disease?**

Mushrooms may be rich in vitamins, minerals, and bioactive compounds such as polysaccharides, but recent research indicates that the fungi may not measure up to claims that they protect against cardiovascular disease and type 2 diabetes.

Investigators from Harvard Medical School and Harvard’s T.H. Chan School of Public Health noted that evidence from human studies to support mushrooms’ cardiometabolic benefits is limited. So they turned to 2 large, prospective, long-running cohort studies—the Nurses’ Health Study and the Health Professionals Follow-up Study—to examine whether eating mushrooms may reduce cardiometabolic disease risks or affect related biomarkers such as low-density lipoprotein (LDL) cholesterol.

Their analysis involved 67,139 women, 43,541 men, and more than 2 million person-years of follow-up. Based on food-frequency questionnaires, the investigators separated participants into categories according to how often they ate mushrooms. The cardiometabolic disease biomarkers they evaluated in addition to LDL cholesterol included total and high-density lipoprotein cholesterol, triglycerides, C-reactive protein, and C peptide.

Among participants who ate 5 or more servings of mushrooms per week, the investigators found no difference in risk of cardiovascular disease or type 2 diabetes compared with those who ate mushrooms less than once a month. They also found no association between mushroom consumption and disease biomarkers.

The investigators did, however, note limitations: Mushroom consumption in their study was low; about half the participants ate them less than once a week. In addition, they assessed mushroom consumption only once, at baseline. “Given the wide popularity of mushrooms and the growing interest in their potential clinical effects, more prospective cohort studies addressing the limitations of this study are warranted,” the researchers wrote.

**Heritable Genome Editing—Edited Eggs and Sperm to the Rescue?**

Eli Adashi, MD, MS; I. Glenn Cohen, JD

“[W]e might anticipate the in vitro culture of germ cells . . . coupled with recognition, selection and integration of the desired genes . . .” Nobel Laureate Joshua Lederberg, PhD (1963)

**Heritable genome editing** is widely predicted to render inborn afflictions a thing of the past. Topping the list of edit-worthy maladies are single-gene disorders for which preimplantation genetic diagnosis is unworkable. In addition, an insufficient number of viable embryos without the disease mutation is an important limitation in preimplantation genetic diagnosis, and in such cases, heritable genome editing might offer an alternative strategy.

Constraints along these lines have frequently undermined some families’ attempts to have a baby—a “savior sibling”—who could serve as a stem cell donor to a sick older sibling who might benefit. Heritable genome editing could also be brought to bear on disease-predisposing gene variants, such as a variant of the APOE gene that contributes to Alzheimer disease risk; a variant of the LPA gene that contributes to atherosclerotic cardiovascular disease; a variant of the MYPBC3 gene that causes hypertrophic cardiomyopathy; and variants in BRCA genes that increase breast and ovarian cancer risk. Currently, the focus of preclinical research, with safety and efficacy in mind, heritable genome editing remains years away from the clinic.

Preclinical research efforts to replace mutant alleles with wild-type counterparts have thus far been limited to human embryos. Such efforts have formidable technical challenges, including introduction of unintended genomic insertions, deletions, and rearrangements, which cannot be tolerated in the clinical context. Nothing less than unyielding editing precision is required to preclude cross-generational harm. An additional challenge to editing the human embryo is the uniformity imperative—ensuring that all the embryo’s cells are appropriately edited. Failure to edit the entire cellular complement of the embryo to exclude mosaicism (in this case, a mixture of edited and unedited cells) is clinically inviable. One final challenge of note is the required validation of edited embryos as transfer eligible. Impeccable editing fidelity as well as uniformity must be documented prior to embryo transfer. At present, however, such reliable assessment is technologically infeasible, and accomplishing this goal may require new technologies.
Apart and distinct from the technical hurdles, editing the genome of the human embryo is also subject to political and doctrinal opposition, which likely gave rise to the statutory federal moratorium now in effect. Under the Consolidated Appropriation Act of 2016, the moratorium prohibits the US Food and Drug Administration from addressing research “in which a human embryo is intentionally created or modified to include heritable genetic modification.” Expounding on the bill in question, Rep Harold D. Rogers (R, Kentucky) noted that it “preserves the sanctity of life,” adding “new provisions prohibiting genetic editing of human embryos.” Rep Robert B. Aderholt (R, Alabama) said that “prohibition on gene editing of human embryos...is a tremendous victory for those who are concerned about life.” Given that the prospect of editing the human embryo genome is caught up in the debate over abortion, proponents of gene editing will be hard-pressed to secure the broad political support required for its actualization.

In light of such technical, political, as well as doctrinal challenges, genomic editing in the human embryo thus faces an uphill struggle, and it is against this backdrop that the possibility of editing human eggs or sperm first came to the fore. Given that the editing of eggs and sperm is not mentioned in the statutory federal moratorium, limited political and doctrinal opposition to this approach may be assumed. An additional advantage of this task is that it avoids the possibility of embryonic mosaicism. The feasibility of assessing the quality of the editing process constitutes yet another upside.

During the 2015 International Summit on Human Gene Editing, scientists reported that editing of mouse spermatogonial stem cells corrected a cataract-causing mutation. Further progress, however, has been sparse. Held back by the requisite testicular transplanting of edited spermatogonial stem cells, only a limited body of experimental work followed. There has been a comparably modest body of work dedicated to the editing of maturing eggs.

The successful editing of human gametes, it would seem, may have to await the materialization of a rapidly evolving scientific field, in vitro gametogenesis (IVG), which is poised to convert somatic cells (such as skin) to induced pluripotent stem cells, and thereupon to mature eggs or sperm. Editing of IVG-derived egg or sperm precursors and their validation by whole-genome sequencing should prove eminently feasible. Correctly edited clones of eggs or sperm could then be selected for eventual use during in vitro fertilization. At this point, scientists have generated human primordial germ cell-like cells and oogonia in vitro. However, the in vitro reconstitution of the entire cycle of the human germline remains to be accomplished. Given the anticipated advantages of editing the genome of IVG-generated human eggs or sperm, this innovation may well be worth the wait.

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