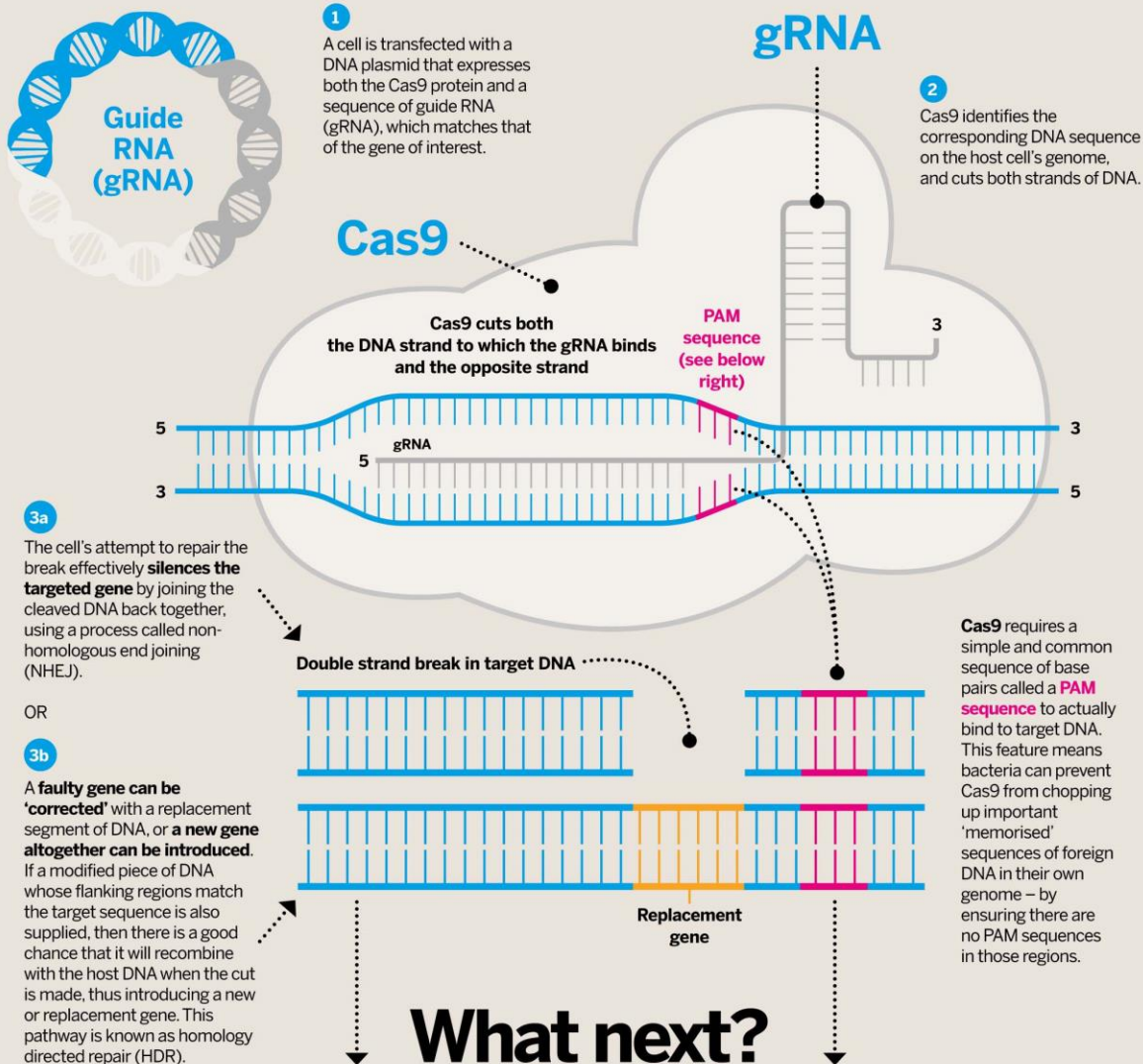


Applications

- How it works; and see <https://news.aamc.org/research/article/crispr-gene-editing-revolution>,
<https://www.addgene.org/crispr/guide/>

CRISPR-Cas9

How the genome editor works



FOOD AND LIVESTOCK MODIFICATION

Researchers have already created plants and mammals with edited genomes. It is hoped such technology could help boost productivity and improve food security.



GENE DRIVE

Some genes are more likely to be passed on than others. If an 'edit' is linked to these genes, it will quickly spread through a wild population. That sounds alarming, but could help eradicate malaria-carrying mosquitos.



GENE THERAPY

Genetic disease could be treated by introducing gene editing systems into affected cells. Researchers in the USA are trialling this to treat HIV by knocking out the gene for the specific T-cell receptor that the virus targets.



HUMAN GERM LINE

Modifying human embryos, sperm or eggs would introduce changes to the genome of future generations. Some argue that other techniques, such as embryo screening, can just as effectively prevent genetic disease.



DESIGNER ORGANISMS AND MORE...

In future, could babies be 'designed' with a genome of our choosing? Could amateur biologists do their own gene editing outside regulatory systems?

2. Alexandra Ossola, *Betting on the first disease to be treated by gene editing*, CNBC Mar. 15 '17
<https://www.cnbc.com/2017/03/13/betting-on-first-disease-to-be-treated-by-crispr-genetic-engineering.html>
[University of Western Ontario associate professor of biochemistry David] Edgell thinks CRISPR treatments could be available within the next two to three years, with modified T-cells used to treat some types of cancer (there are already clinical trials for lung cancer in China, and a similar one slated to take place at the University of Pennsylvania was approved last June by the National Institutes of Health).

3. Susan Scutti, *Medical first: Doctors attempt to gene-edit a living person's DNA*, CNN, Nov. 15 '17
<http://www.cnn.com/2017/11/15/health/first-in-body-edit-dna>

A man may soon be forever free of the previously incurable disease he was born with 44 years ago. On Monday, in a medical first, Brian Madeux received an experimental in-body gene-editing treatment intended to cure him of Mucopolysaccharidoses II, known as MPS II or Hunter syndrome, a rare disorder that causes progressive damage to the body's cells. From Madeux's point of view, the revolutionary treatment appears anything but: It was a simple matter of getting hooked up to an IV, which delivered a gene editor into his bloodstream along with copies of a corrected gene to replace the mutation he carries that is responsible for the disorder. "The infusion takes place for anywhere from two to three hours. And that's it," said Dr. Edward Conner, senior vice president and chief medical officer of Sangamo Therapeutics, maker of the new therapy. "We're very hopeful."

4. Antonio Regalado, *Engineering the Perfect Baby*, Technology Review Mar. 5 '15

<https://www.technologyreview.com/s/535661/engineering-the-perfect-baby/>

[G]erm-line engineering is much further along than anyone imagined... [Merle] Berger [one of the founders of Boston IVF, a large network of fertility clinics] predicts that repairing genes involved in serious inherited diseases will win wide public acceptance but says the idea of using the technology beyond that would cause a public uproar because "everyone would want the perfect child": people might pick and choose eye color and eventually intelligence.

5. Anne-Marie Guarnieri, *The Future of Anti-Aging*, Harper's Bazaar Oct. 27 '17

<http://www.harpersbazaar.com/beauty/skin-care/a12776110/future-of-anti-aging/>

Many CRISPR human trials are currently being done in China on patients with HPV, HIV, and lung cancer... As to whether CRISPR will be used for vainer pursuits—think curing baldness, eliminating gray hair, erasing wrinkles—Robinton, 30, is optimistic. "This isn't the first time that biotech has invaded the beauty space," she says. "It's not [yet] real, but it's our hopeful reality."

Three Overarching Halachic Considerations: Risk, Minority and Kilayim

Case 1: Healing a Defect

6. Talmud, Berachot 19b

גדול כבוד הבריות שדוחה [את] לא תעשה שבתורה. ואמאי? לימא אין חכמה ואין תבונה ואין עצה לנגד ד' (משלי כא)! תרגמה רב בר שבה קמיה דרב כהנא בלאו דלא תסור....

"Dignity is so great that it overrides a biblical prohibition." But why not apply Mishlei 21:30, "There is neither wisdom nor understanding nor counsel opposite Gd!" Rav bar Sheva explained before Rav Kahana: The prohibition here is that of, "Do not stray [from the words of the sages]."...

7. Rabbi Yehoshua Neuwirth (20th century Israel), Shemirat Shabbat k'Hilchatah 34: note 52

ושמעתי מהגרש"ז אויערבך שליט"א דכל שיש בו משום כבוד הבריות כגון שהליחה נוזלת לו מן האף יש להקל טפי
I have heard from Rav Shlomo Zalman Auerbach that where dignity is involved, such as the liquid is running from his nose, there is room for greater leniency.

Preface to Case #2: What is the halachic weight of "Jewish Values"?

8. Rambam (12th century Egypt), Mishneh Torah, Hilchot Maachalot Asurot 17:29-30

אסרו חכמים מאכלות ומשקין שנפש רוב בני אדם קיהה מהן כגון מאכלות ומשקין שנתערב בהן קיא או צואה ולחה סרוחה וכיוצא בהן... וכן אסרו לאכול בידיים מסואבות מזהמות, ועל גבי כלים מלוכלכים, שכל דברים אלו בכלל "אל תשקצו את נפשותיכם"...

The sages forbade food and beverages from a person recoils, such as food and beverages mixed with vomit, excrement, foul liquid and the like... And they also forbade eating with dirty hands, or on dirty dishes. All of this is included in, "Do not make yourselves disgusting." ...

9. Rambam (12th century Egypt), Sefer haMitzvot Aseh 8

והמצוה השמינית היא שצונו להדמות בו יתעלה לפי יכלתנו והוא אמרו (תבוא כח) "והלכת בדרכיו..." שענינו להדמות בפעולות הטובות והמדות החשובות שיתואר בהם הקל יתעלה על צד המשל. יתעלה על הכל עילוי רב:

The eighth commandment is that He commanded us to resemble Him to the extent possible, as it says, "And you shall walk in His ways."... This means to resemble via good activities and important traits with which Gd is described in a non-literal way; He is elevated far above all.

10. Rambam (12th century Egypt), Mishneh Torah, Hilchot Shecheinim 12:5

המוכר קרקע שלו לאחר יש לחבירו שהוא בצד המצר שלו ליתן דמים ללוקח ולסלק אותו... משום שנאמר "ועשית הישר והטוב"...

When one sells his land to another, his neighbour may pay the buyer and remove him... for it says, "And you shall do the right and the good."...

11. Rabbi Moshe Chaim Luzzatto (18th century Italy), *Mesilat Yesharim*, Perek 13

אחר שהתבאר לנו היות כל עניני העולם נסיונות לאדם... והתאמת לנו גם כן רוב חולשת האדם וקרבת דעתו אל הרעות, יתברר בהכרח שכל מה שיוכל האדם להמלט מן הענינים האלה ראוי שיעשהו, כדי שיהיה נשמר יותר מן הרעה אשר ברגליהם. כי הנה אין לך תענוג עולמי אשר לא ימשוך אחריו איזה חטא בעקבו...

Now that it has been clarified for us that all of this world's affairs are tests for people... And humanity's great weakness and its tendency toward evil has also been shown to be true, it must also be clear that one must flee from these tests to the extent possible, so as to be shielded from the evil they bring. No pleasure in the world fails to bring sin with it...

12. R' Aharon Lichtenstein, *Does Judaism Recognize an Ethic Independent of Halakhah?* (Leaves of Faith Chap. 2)

[I]f we mean that everything can be looked up, every moral dilemma resolved by reference to code or canon, the notion is both palpably naïve and patently false. The Hazon Ish, for one, and both his saintliness and his rigorous halakhic commitment are legend, had no such illusions. "Moral duties," he once wrote, "sometimes constitute one corpus with halakhic rulings, and it is Halakhah that defines the proscribed and permitted of ethical thought." Sometimes, but not, evidently, always. There are moments when one must seek independent counsels.

13. Shemot 18:20

וְהוֹדַתְתָּ אֹתָם אֶת הַחֲקִים וְאֶת הַתּוֹרֹת וְהוֹדַעְתָּ לָהֶם אֶת הַדֶּרֶךְ יִלְכוּ בָּהּ וְאֶת הַמַּעֲשֵׂה אֲשֶׁר יַעֲשׂוּ:

And you shall warn them of the laws and *Torot*, and you shall inform them of the path on which they shall walk and the deed they shall perform.

14. Talmud, Bava Metzia 30b

"והודעת להם" זה בית חייהם, "את הדרך" זו גמילות חסדים, "ילכו" זה ביקור חולים, "בה" זו קבורה, "ואת המעשה" זה הדין, "אשר יעשון" זו לפנים משורת הדין.

"And you shall inform them" is a livelihood. "Of the path" is acts of kindness. "They shall walk" is looking after the sick. "On which" is burial. "And the deed" – This is justice. "They will perform" – This is to transcend the line of the law.

15. Rabbi Moshe Chaim Luzzatto (18th century Italy), *Mesilat Yesharim*, Perek 13

ואם תשאל ותאמר, אם כן, איפוא, שזה דבר מצטרך ומוכרח, למה לא גזרו עליו החכמים כמו שגזרו על הסייגות ותקנות שגזרו? הנה התשובה מבוארת ופשוטה, כי לא גזרו חכמים גזרה אלא אם כן רוב הציבור יכולים לעמוד בה, ואין רוב הציבור יכולים לעמוד בה, ואין רוב הציבור יכולים להיות חסידים, אבל די להם שיהיו צדיקים.

And if you will inquire and say: If it is so, that this is necessary and required, why did the sages not decree it as they decreed other protections and enactments? The answer is clear and simple: the sages did not issue a decree unless most of the community could bear it. Most of the community could not bear this, and most of the community cannot be pious; it is enough that they be righteous.

16. Dr. Jim Sabin, *What if Madoff Took an Ethics Class?*

<https://healthcareorganizationalethics.blogspot.ca/2009/03/what-if-madoff-took-ethics-class.html>

In medical ethics teaching, most time is spent on teasing out the pros and cons of complex ethical conundrums. But in real life recognizing and acknowledging that there is a conundrum that requires contemplation is as important as the way we reason about it.

17. Rabbi Aharon Lichtenstein, *Religion and Morality*, pg. 123 (*By His Light*, Chapter 6)

Surely, in relating to Halakha, including those areas which one may find morally difficult, there is some role for conscience, some role for the goodness in us, particularly in an interpretive capacity. Conscience does and legitimately can have a role in helping us to understand the content and substance of the *tzav*.

18. Rabbi Vidal of Toulouse (14th century Spain) *Maggid Mishneh*, *Mishneh Torah*, *Hilchot Shecheinim* 14:5

וכן אמרה "ועשית הישר והטוב" והכוונה שיתנהג בהנהגה טובה וישרה עם בני אדם. ולא היה מן הראוי בכל זה לצוות פרטים לפי שמצוות התורה הם בכל עת ובכל זמן ובכל ענין, ובהכרח חייב לעשות כן, ומדות האדם והנהגתו מתחלפת לפי הזמן והאישים.

And so the Torah says, "And you shall do the right and the good," meaning to act in a way that is good and right with people. It would not have been appropriate to instruct specifics, because the Torah's mitzvot apply at all times and in all matters, as they must be, while a person's traits and behaviour changes with times and personalities.

19. Rabbi Meir Simchah haKohen (19th century Poland), *Or Sameach* to *Mishneh Torah*, *Hilchot Talmud Torah* 1:2

ונמצא מצוות ת"ת אשר בוודאי אם יבקש האדם טרף ומזון בכ"ז אינו נחשב למפריע מצוות ת"ת, ואספת דגניך כתיב (דברים יא, יד), וכן למשל אדם חלוש המזג, וכן כל אחד לפי ההכרחיות שלפי הרגלו, וכן לפי טוהר נפשו של אדם. כי אינו דומה בחיוב ת"ת האיש אשר נפשו מרגשת בשכלה הזך ונקשרה בעבודת אהבה לתלמוד תורה, לאיש אשר כוחות נפשו נרפים ועצלים...

We see then in the mitzvah of Torah study that certainly, one who seeks food is not viewed as interrupting the mitzvah of Torah study; the Torah says, "You shall gather your grain." And so, too, for example, one of weak constitution, and so for each person with the needs of his custom and the purity of his spirit. The duty of Torah study is not the same for someone who appreciates its pure intellect and is bound with ropes of love to Torah study, and for someone whose spiritual abilities are weak and lazy...

20. Rabbi Yosef Dov Soloveitchik (20th century USA), *Halakhic Morality* pg. 186

The halakhic law was addressed to the eternal ideal Jew, purged of historical evanescence and transience, detached from continuous transition, immutable and enduring through the generations. The moral obligation, in contrast, was handed down to the concrete individual, to each Jew as a separate, autonomous, one-timely and singular being living in a changing, history-making world. Each individual fulfills his moral commitment in his own private and unique fashion...

Value #1: Beautification

21. Rabbi Eliezer Waldenberg (20th century Israel), *Tzitz Eliezer* 11:41:9

ואך מגוחך הוא לבוא ולהציע להתיר ניתוח כזה לנשים בגבוב קולות עפ"י מדרשים שונים המהללים היופי לנשים, ואין כדאי אפ' להשיב ע"ז דאין לבכזאת מקום בהל' כלל... ורק באופן מליצי יש להשיב ע"ז בדברי שלמה המלך ע"ה שהטיף ברוח ד' אשר בקרבם ואמר: שקר החן והבל היופי אשה יראת ד' היא תתהלל, וכל אשר יראת ד' נגע בלבה לא תלך שולל אחרי להיטת עשיית נתוחים פלסטיים כאלה לשם יפוי וגוי בלבד ושע"פ רוב המה רק לפי מראה עינים והלך נפש של בני האדם שאין אחד דומה למשנהו... ואם אין להטריח את הקונה לשנות את הטבע (יעו"ש במהרש"א ד"ה עמי היתה) על אחת כמה שאין לו לאדם להתחכם בעצמו לשנות הטבע בפעולות כאלה, והר"ז כאומר לאומן שעשאו כמה מכוער כלי זה שעשית (עיי' תענית ד' כ' ע"ב).

It's entirely ridiculous to suggest to permit such surgery for women by amassing leniencies from various midrashim which praise women's beauty. It is not even worth responding to this, for such things have no place in law at all... Only as a homiletic would I respond with the words of King Solomon, who spoke with his Divine inspiration, saying, "Charm is false, and beauty is vain; a woman who reveres Gd is to be praised." Anyone with reverence for Gd in her heart would not stray after such fads of plastic surgery for aesthetics alone, most of which is just for appearances and whims of human beings, no two of whom [were created to] look alike... If one should not trouble Gd to alter nature, how much more so should one not try to be clever and change nature with such activities, which would be like telling the Craftsman who made him, "How ugly is this vessel You made!"

22. Talmud, Bava Batra 58a

הכל בפני שרה כקוף בפני אדם חוה כקוף בפני אדם בפני אדם בפני שכינה כקוף בפני אדם
People compared to Sarah are as a monkey compared to a person. Sarah compared to Chavah is as a monkey compared to a person. Chavah compared to Adam is as a monkey compared to a person. Adam before the Shechinah is as a monkey compared to a person.

23. Rabbi Eliyahu Cramer (Vilna Gaon, 18th century Vilna), Kol Eliyahu to Parshat Vayetze

שקר החן והבל היופי היינו כשהן בלתי יראת ד', והם כנזם זהב באף חזיר, אבל אשה יראת ד' היא תתהלל ר"ל דגם החן והיופי תתהלל.
"Charm is false and beauty is vain" when they lack reverence for Gd; then these are like "a gold ring in the nose of a pig." But "A woman who reveres Gd is praised," meaning that then even the charm and beauty are praised.

Value #2: Creating

24. Ramban (13th century Spain), Vayikra 19:19

המרכיב שני מינין, משנה ומכחיש במעשה בראשית, כאילו יחשוב שלא השלים הקב"ה בעולמו כל הצורך ויחפוץ הוא לעזור בבריאתו של עולם להוסיף בו בריות.

One who grafts two species changes and contradicts Creation, as though he thinks that Gd did not complete his world with every need, and he wishes to aid the creation of the world by adding creatures.

25. Israeli Chief Rabbi Yisrael Meir Lau, press release, 2003

The moment medical science tries to take upon itself duties and areas which are not its responsibility - such as shortening life, cloning or creating life in an unnatural way - we must set down borders in order not to harm the Jewish basic belief that there is a creator of the universe in whose hands life and death are placed.

26. Rabbi Yehudah Loeb (Maharal, 16th century Poland, Moravia, Prague), Be'er haGolah 2:10

כמו שהיה כח הטבע פועל בגזירת ד' יתברך, והיה כח הטבע פועל בששת ימי ראשית מה שראוי אל הטבע, כך האדם מצד השכל אשר בו, שהוא על הטבע, ופעולתו דבר שאינו טבעי...

Just as Nature operates at Divine decree, and Nature functioned during the six days of Creation as is appropriate for Nature, the same applies to the actions of a person, with his brain which is above Nature and with his deeds which are not of Nature...

27. Rabbi Yosef Dov Soloveitchik (20th century USA), *Halakhic Man* (Kaplan translation, pp. 100-101)

The Scriptural portion of the creation narrative is a legal portion, in which are to be found basic, everlasting halakhic principles... If the Torah then chose to relate to man the tale of creation, we may clearly derive one law from this manner of procedure – viz, that man is obligated to engage in creation and the renewal of the cosmos.

28. Talmud, Sanhedrin 65b

אמר רבא אי בעו צדיקי ברו עלמא שנאמר כי [אם] עונותיכם היו מבדלים ביניכם לבין אלקיכם.

Rava said: If the righteous wished, they could create worlds, as Yeshayah 59:2 says, "For only your sins separate between you and your Gd."