

Web-based tool makes vaccine development faster and more accurate

March 15 2023

(a)

1. Provide the RNA or DNA sequence in the box

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TTGAACATTTCAGTCTCTTGTCCCTAAGGCAACCAGAAGCCG
GTACAGTGGATTCTGAAGGACACTGTTCCAGCAAATGCGGGA
TGTGCTTGGGACATTTGACACTGTCCAATAATAAACTTCTC
CCCTTTGCTGCTGCCCCACAGAACAGAGTAGGATGCAATTTT
CCTCATTGACTGTGAATGTGAGAGGATCAGGGTTGAGGATAC
TGGTAAGAGGCAATTCCTCAGTATTCAATTACAACAAGGCAAC
CAACGACTTACAGTTCTTGGAAAGGATGCAGGTGCATTGAC
TGAAGATCCAGATGAAGGCACATCTGGGGTGGAGTCTGCTGT
CCTGAGAGGATTCTCATTTGGCCAAAGAACAGAGATAT
GGCCACGATTAAGCATC
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FILL WITH EXAMPLES

2. Select the organism for codon usage table

Homo sapiens

SUBMIT RESET

(b)

The codon deoptimized sequence is:

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ATG GC ATG TA CC AT AC GC GA AA G- ATA ATG GA ATG AT CC GA G- AAT GAA CAA GG CAA AC CT TGG TAA AAC AA- GAT GC
GC TC GA CG GT ATG GTA TCC CC CT GC GTA AC TGG TGG AAT G- AAT GG CC AC AC TAA AC GT CAT TA CC AA- GTA TAT AAA AC TAT
TT GAA AA- GT GAA G- AAA CAT GGT AC TT GC CC GT CA TT G- AAT CAA GT AAA ATA G- G- GT GAT AC AA- CC G- CAT GC
GAT CT GC G- AA- GA- GC CA- GAT GT AT ATG GAA GT GT TT CC AAT GAA GT GG GC G- ATA CT AC TC GA- TC CA- CT GC ATA AC
AAA G- AA- AAA GAA GA- CT CA- GAT TGT AAA AT GC CC G- ATG GT GCG TA- ATG CTA GAA G- GAA G- GT CGT AAA AC G- TTT CT CC GTA
GC GG GG AC GG T- GT TAT AT GAA GT G- CA- TA AC CAA GG ACG TG- TGG GA- CA- ATG TA- AC CC GG GG- GAA GT G- AAT GAT GAT
GT G- CAA G- AT AT GC GC G- AA- ATA GTA G- G- GC G- GT TC GC GA- CC G- TA GC TC CT G- GAA ATG TG CA- G- AC CA-
AT GC GG GTA G- ATG GT GA- AT CT G- CA- AAT CC AC GA- GAA CAA GC G- ATA TG AA- GC G- ATA GG G- AT- AT- TCC TC
TT G- TTT GGT GG TT AC TT AAA G- AC G- GG TC TC G- AA- AAA GAA GAA GAA GT CTA ACG GG AA- CT CAA AC CT- AAA ATA G- GTA
CAT GAA GG TAT GAA GAA TT AC ATG GT GG G- GC AC GC AT CT G- AA- GC AC G- AT- ATA GTA G- GG G- GA-
GA CA- TC AT GC GA- GC ATA AT GT GC ATG GTA TT TC CA- GA- GAT TG ATG AT AA- GC GT G- GG GAT CT AA- TTT GT AAT G- GC
AA CA- CG CT AA- CC ATG CA- CAA CT G- G- CAT TT CAA AAA GAT GC AAA GT CT AA- TGG GG AT GAA TC AT GAT AAT GT ATG
GC ATG ATG G- AT C- CC GA- ATG AC CC G- ACG GA- ATG TCG CT G- GG ATA G- G- AA- ATG GG GTA GAT GAA TA- TCC T- ACG GA-
G- GT GTA GT T- AT G- CG TTT TA G- GT G- GAT CAA G- G- AA- GTA CTA G- TC CC GAA GAA GT G- GAA ACG CAA GG AC GA- AA-
AA AC ATA AC TAT TCG TC T- ATG ATG TGG GA- AT- AAT GG CC G- TC GT CTA GT AA- AC TAT CAA TGG ATA AT- AA- TGG GAA AT GT
AAA AT CAA TGG TC CAA GAT CC AC ATG TA TA AA- AAA ATG GAA TTT GAA CC TTT CA- TC CT GT CC AA- G- AC G- T- CG TA- T- GG
TT GTA G- AC CT TT CA- CAA ATG CG GAT GT CT GC AC TTT GA- AC GT CAA ATA ATA AAA CT CT CC TTT GC GC CC CC GAA CA-
T- ATG CAA TTT TC T- AT G- AT AAT GT G- G- TCG GG G- G- ATA CT GTA G- GG AAT TC CC GTA TT AAT TA- AA- AA- GC AG
AAA CG CT AC GT CT G- AA- GAT GC GGT GC G- AC GAA GAT CC GAT GAA GG AC TC GG GT GA- TC GC GT CT G- GG TTT CT AT-
T- GG AAA GAA GA- AA- G- TAT GC CC GC TA G- AT
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(c)

Result Statistics:

No. of Codons	Codon changes	% codon changes	NTs	NTs changes	% NTs changes	% GC WT	% GC CD
660	457	69.24	1980	556	28.08	44.75	42.83

Codon deoptimized Protein sequence:

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M R Y P I A D K R I M D E X P E R N E C Q T L S K T D A G S D R V M V S P L S V E M W N N G P I T T S T V Y P K V Y K T Y E E V E R L K H G T E G P V H F R N O K I R R R V D T N P G A D S A K E A Q D V I M E V W F P N E V G A R I L T S E S Q U A I I K
K E E L Q D C K E A P E M V A N L E E F L V R K T F L P A G G T G S V Y E V L H L C Q T D E Q N T P G E V R N D D Q S L T I A A R N I V R R A V S A D P L A S L L E M C H S T Q I G G V R V O I L R G N P T E C V I I C K A R I S L R I S S E S F S F G
G R T E K R T S G S S V K K E E E Y L T Q N Q Y T K I I V H E S Y E E E T V G R R A T A L L R K A T R R L T Q L I V S G R D E Q S I A E I I V A H V F S Q E C Q I K A V R G L N F N R A N Q R L N P R Q L L R E Q K D A V E R Q N G E S T G N G S I G I I
P D M T P S T E H S E R G I R V S K H G V D E Y S S T E R V V S I D R F L R V S D O R G N V L S P E E S E T C G T E K L I I T Y S S S M N N E N G P E S V L V I T V Q W I E R N H E I V I Q N Q D R T L V N K M E F E P S S I V P K A T R S R Y S G V R T L E Q Q
M D V L G T D T V Q I I K L L P A A P P E Q S H M Q F S S L T V V A G S G L R I V R S P V E M Y N K A T R L E V L G K R A L T E D E D E S T S G V E S A V L R G F I L L G K E D K N Y P A L S I
```

The codon usage table used: Homo sapiens

Download the results

An example of how CoDe works. Users input the genetic sequence they want to deoptimize and CoDe then identifies which nucleotides to change. Credit: Texas Biomed

A new software tool developed by Texas Biomedical Research Institute

and collaborators can help scientists and vaccine developers quickly edit genetic blueprints of pathogens to make them less harmful.

The tool, called [CoDe](#)—short for Codon Deoptimization—enables users to make precise edits to a genetic [code](#) to make [genes](#) less functional—in other words, to deoptimize the genes.

Often, vaccine developers want to optimize or turn up expression of certain genes, and there are plenty of software tools to help with that. But for some types of vaccines, it is critical to deoptimize (turn down) certain genes, to make the vaccines safe and effective.

"There were no tools to help with deoptimization until now," explains Texas Biomed Professor Luis Martinez-Sobrido, Ph.D., who led the team behind CoDe.

Dr. Martinez-Sobrido is an expert in virology and vaccine development. He teamed up with bioinformatics experts at the Indian Institute of Technology, Madras and a virologist at the Center for Animal Research in Spain to build CoDe. They have recently described their tool in the journal *Bioinformatics Advances*.

Turning down [gene expression](#) can be useful for a wide range of research, and is particularly important for developing live attenuated vaccines. This type of vaccine includes the full genetic sequence of a virus, rather than just a small part of the virus. But the virus has been attenuated, or tweaked, to not cause disease. This is a common vaccine platform that has been used for influenza, smallpox, yellow fever, and mumps, measles and rubella.

This type of vaccine aims to elicit long-lasting, robust immunity, and it is imperative that the virus has been attenuated enough so that it cannot revert back to its original form.

"With CoDe we can precisely mutate thousands of nucleotides in a [single gene](#), which makes it extremely difficult for the virus to revert," Dr. Martinez-Sobrido says. "It also enables us to modulate gene expression of small sections, rather than knocking out entire genes completely. That is very helpful for vaccine design as well as basic research."

Users tell CoDe which genetic sequence to deoptimize. The program identifies which specific nucleotides (letters) to change within the [genetic code](#), which results in a functional but harmless version of the virus.

A distinctive feature of the program is that it can automatically convert the edits needed to attenuate a [vaccine](#) designed for different species. For example, an [influenza vaccine](#) will differ for pigs versus chickens versus humans.

While designed for viruses, CoDe can easily be adapted for other organisms, such as bacteria.

"Scientists have been waiting for this kind of tool because before they were doing it by hand," explains Tracey Baas, Ph.D., Texas Biomed's Innovations Manager. "This will help them make edits faster, and avoid the potential for mistakes than can occur through human error."

The tool is copyrighted, but freely available for others in academic settings to use.

More information: Divya Sharma et al, CoDe: a web-based tool for codon deoptimization, *Bioinformatics Advances* (2022). [DOI: 10.1093/bioadv/vbac102](#)

Provided by Texas Biomedical Research Institute

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