# Glycation affects translation accuracy

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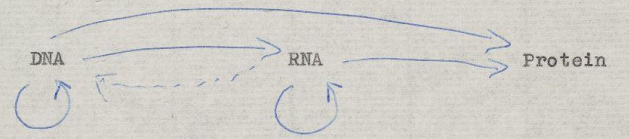
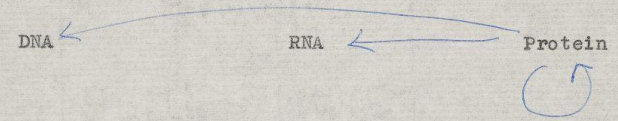
## Ideas on Protein Synthesis (Oct. 1956)

The Doctrine of the Triad.

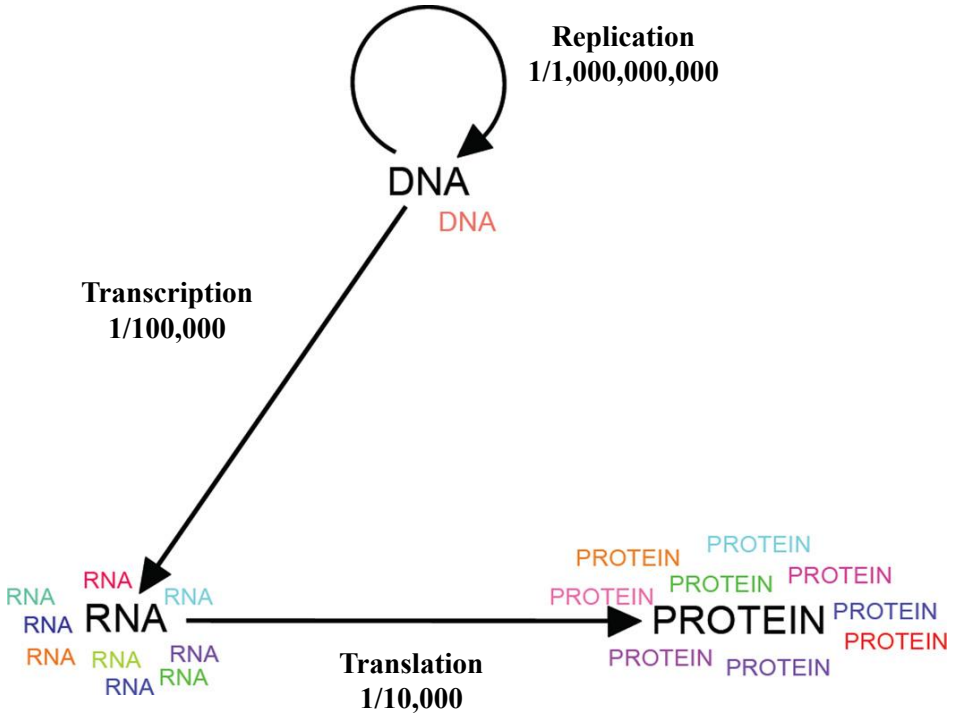
The Central Dogma: "Once information has got into a protein it can't get out again". Information here means the sequence of the amino acid residues, or other sequences related to it. That is, we may be able to have



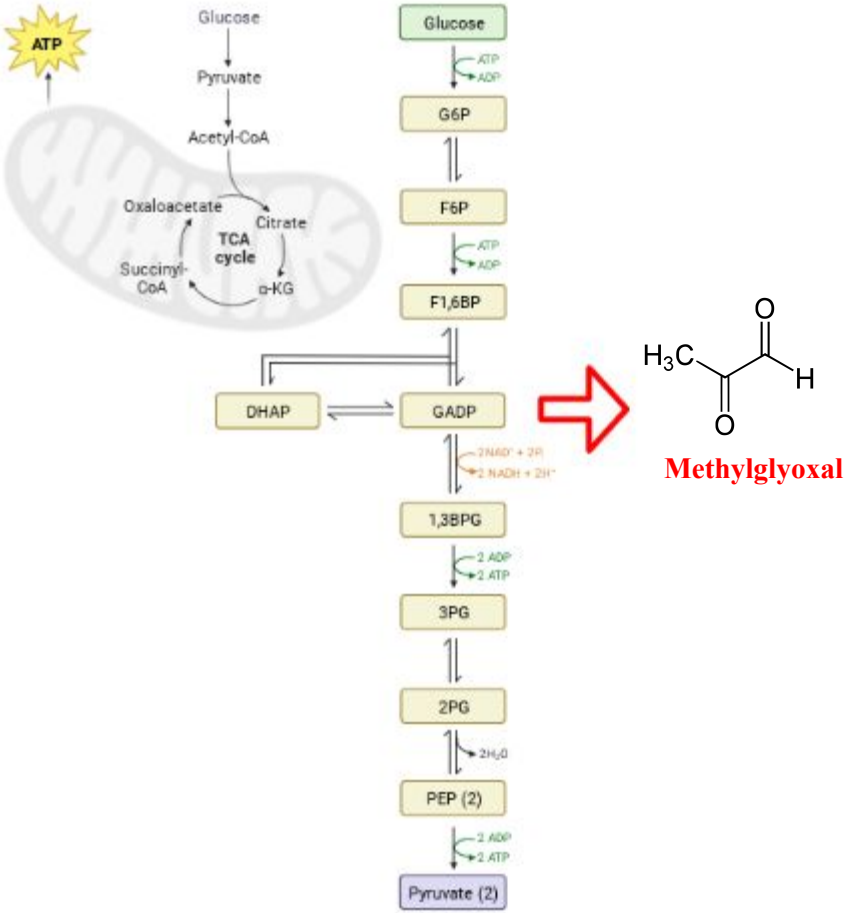

but never




where the arrows show the transfer of information.

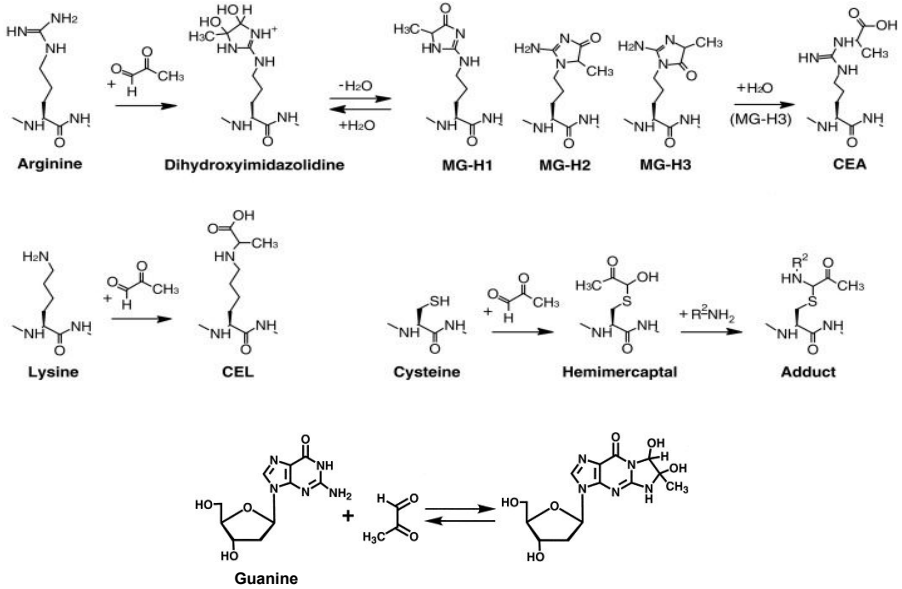



10.1016/j.mib.2015.01.010






**Methylglyoxal**



# Premise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## Activation of the unfolded protein response in high glucose treated endothelial cells is mediated by methylglyoxal

Received: 6 August 2018
Accepted: 21 November 2018
Published online: 27 May 2019

Zehra Irshad[1], Mingzhan Xue[1], Amal Ashour[1,2], James R. Larkin[1,3], Paul J. Thornalley[1,4] & Naila Rabbani[1,5]

- ❑ High glucose leads to increase in methylglyoxal production
- ❑ Methylglyoxal reacts with intracellular proteins
- ❑ Methylglyoxal production/protein glycation are associated with unfolded protein response

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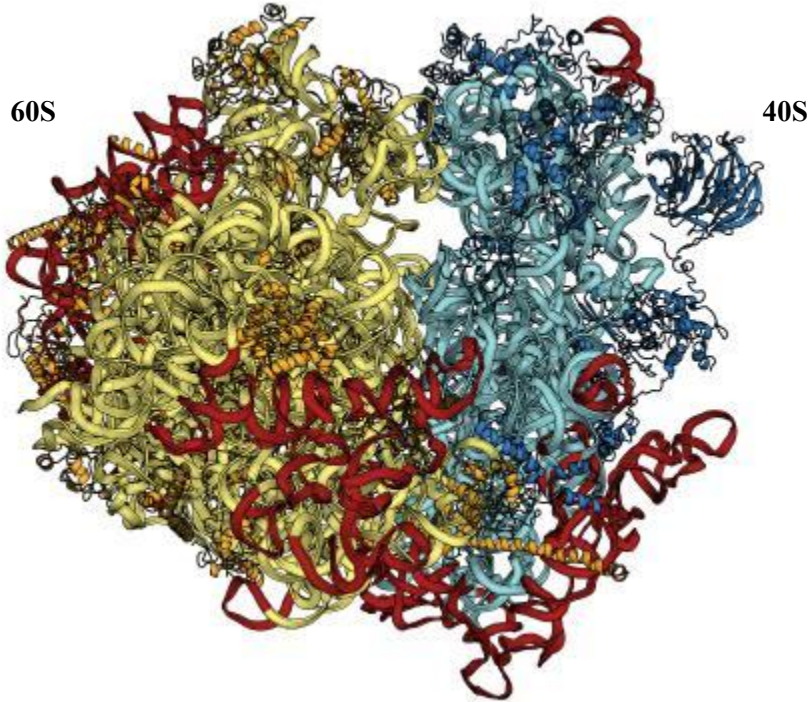
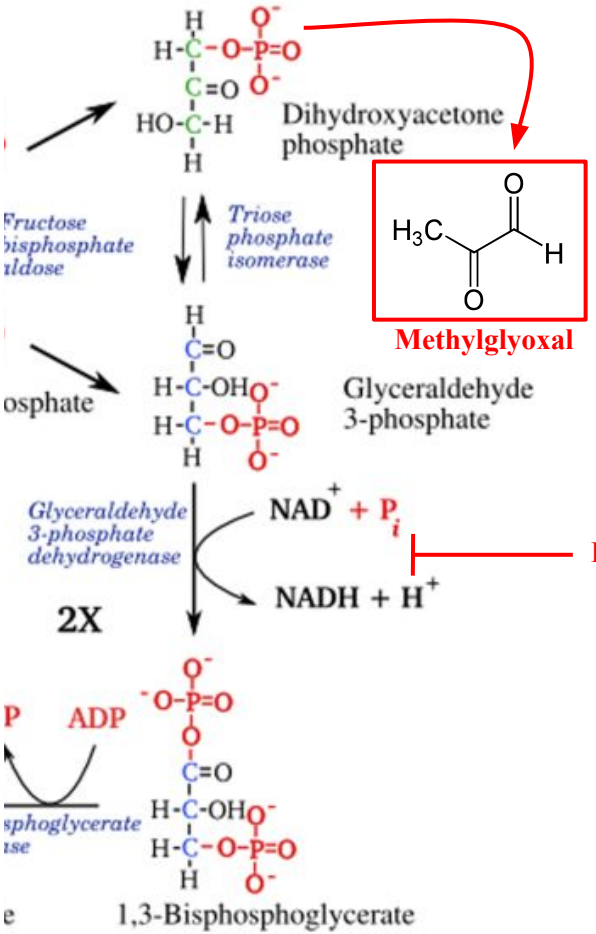
# Ribosome




10.1126/science.1194294

# Hypothesis


- Methylglyoxal indiscriminately reacts with intracellular proteins, including ribosomal components – RP, rRNA
- Glycation of ribosomes alters translation accuracy
- Glycated ribosomes produce misfolding-prone proteins that contribute to UPR




Koningic acid

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Biochimica et Biophysica Acta 1637 (2003) 98–106

BIOCHIMICA ET BIOPHYSICA ACTA
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# Glyceraldehyde-3-phosphate dehydrogenase activity as an independent modifier of methylglyoxal levels in diabetes

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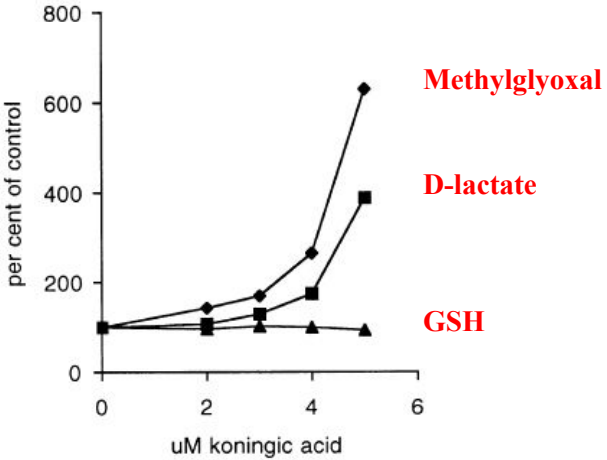
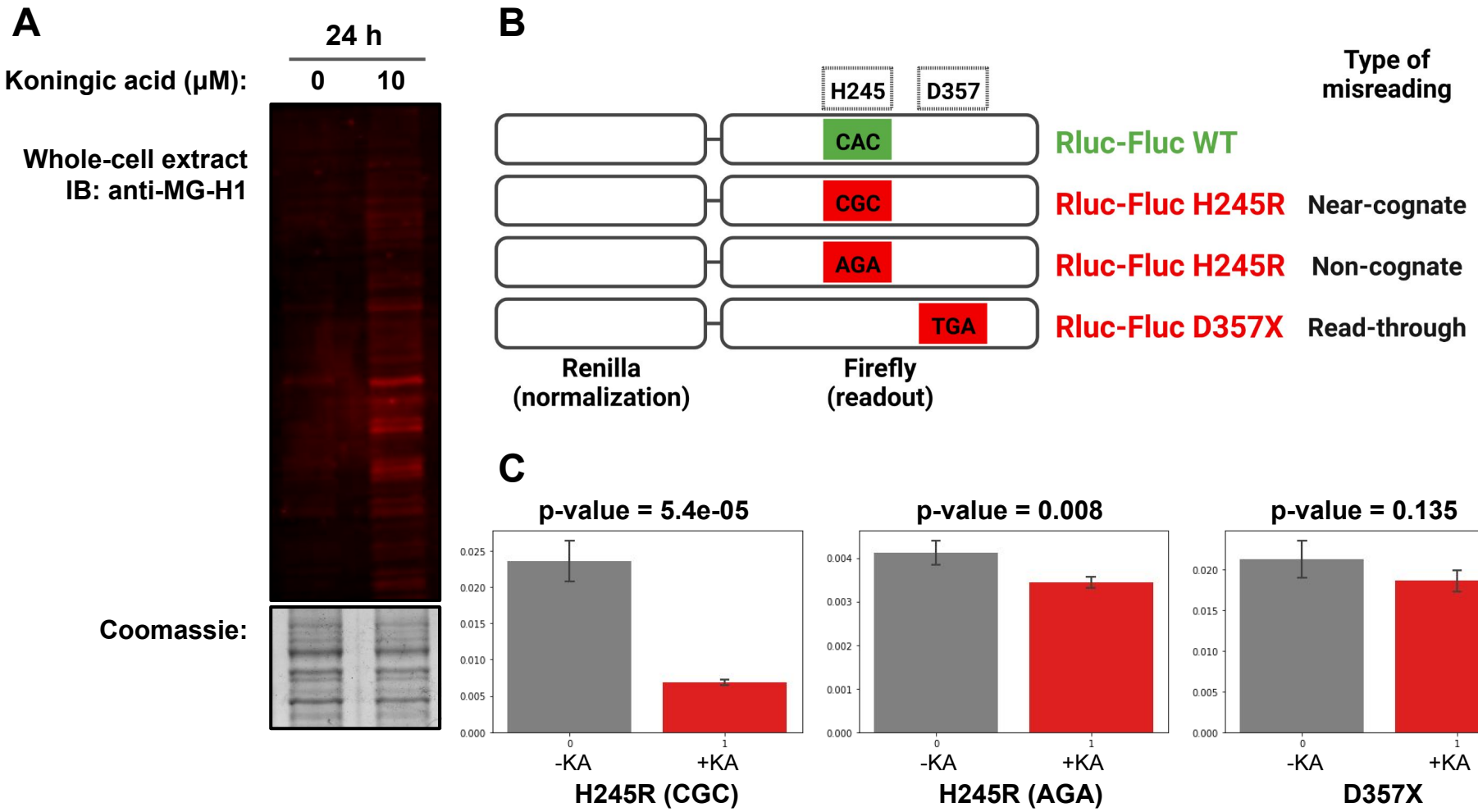
Received 17 April 2002; received in revised form 13 November 2002; accepted 15 November 2002




A
24 h
Koningic acid (μM):
0
10
Whole-cell extract
IB: anti-MG-H1
Coomassie:
B
H245
D357
Type of misreading
CAC
Rluc-Fluc WT
CGC
Rluc-Fluc H245R
Near-cognate
AGA
Rluc-Fluc H245R
Non-cognate
TGA
Rluc-Fluc D357X
Read-through
Renilla
(normalization)
Firefly
(readout)
C
p-value = 5.4e-05
p-value = 0.008
p-value = 0.135
0.025
0.020
0.015
0.010
0.005
0.000
0.004
0.003
0.002
0.001
0.000
0.020
0.015
0.010
0.005
0.000
0
1
-KA
+KA
H245R (CGC)
H245R (AGA)
D357X


**Thank you!**

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