



1
00:00:00,790 --> 00:00:07,320

[Music]

2
00:00:11,470 --> 00:00:09,120

[Applause]

3
00:00:14,470 --> 00:00:11,480

thank you very much the organizers for

4
00:00:18,130 --> 00:00:14,480

the opportunity to speak tell you about

5
00:00:19,390 --> 00:00:18,140

some work that is ongoing so most of

6
00:00:20,620 --> 00:00:19,400

this stuff is not published but we're

7
00:00:23,819 --> 00:00:20,630

getting close so kind of getting excited

8
00:00:26,109 --> 00:00:23,829

I'll try and run you through some things

9
00:00:28,359 --> 00:00:26,119

so I think the main problem that we've

10
00:00:31,630 --> 00:00:28,369

struggled with in early evolution is

11
00:00:33,010 --> 00:00:31,640

that we used to be focusing on how can

12
00:00:35,979 --> 00:00:33,020

we take things like genomes and

13
00:00:37,450 --> 00:00:35,989

reconstruct ancestral States and the big

14

00:00:39,819 --> 00:00:37,460

problem that we've run up against is

15

00:00:41,620 --> 00:00:39,829

that now that we're awash with data the

16

00:00:49,060 --> 00:00:41,630

signal actually seems to be quite poor

17

00:00:51,880 --> 00:00:49,070

so oh sorry yeah so here's just one

18

00:00:54,640 --> 00:00:51,890

example from work that we've done which

19

00:00:57,640 --> 00:00:54,650

is it I threw this in because a lot of

20

00:00:59,680 --> 00:00:57,650

our NA stuff in the meeting but people

21

00:01:01,690 --> 00:00:59,690

have done the same thing for proteins as

22

00:01:04,299 --> 00:01:01,700

well basically what we did was we looked

23

00:01:06,969 --> 00:01:04,309

at the our fam database which is a big

24

00:01:09,039 --> 00:01:06,979

database with 15 million 15 hundred RNA

25

00:01:11,530 --> 00:01:09,049

families and asked well how many things

26
00:01:13,120 --> 00:01:11,540
appear in more than one domain and as

27
00:01:15,220 --> 00:01:13,130
you can see from this Venn diagram the

28
00:01:16,960 --> 00:01:15,230
numbers are very small when you look at

29
00:01:19,210 --> 00:01:16,970
what's actually there and likely to be

30
00:01:21,340 --> 00:01:19,220
conserved you know it's it's basically

31
00:01:22,930 --> 00:01:21,350
stuff associated with the ribosomes so

32
00:01:25,420 --> 00:01:22,940
we've obviously heard quite a bit about

33
00:01:28,719 --> 00:01:25,430
the ribosome and previous sessions and

34
00:01:30,100 --> 00:01:28,729
then our own ASP the tRNAs so this is

35
00:01:34,719 --> 00:01:30,110
sort of stuff you would you would be

36
00:01:35,770 --> 00:01:34,729
able to I think guess from without too

37
00:01:37,270 --> 00:01:35,780
much trouble there's a few other little

38
00:01:39,219 --> 00:01:37,280

details in there but the main point is

39

00:01:40,810 --> 00:01:39,229

that this very little signal there the

40

00:01:43,660 --> 00:01:40,820

signal is consistent with what people

41

00:01:47,350 --> 00:01:43,670

would get when they look at protein data

42

00:01:48,640 --> 00:01:47,360

in genomes but you know that's weaker

43

00:01:50,640 --> 00:01:48,650

sort of say well maybe we can think of

44

00:01:53,230 --> 00:01:50,650

better ways to do that or maybe we can

45

00:01:57,700 --> 00:01:53,240

rethink how we're doing stuff so if the

46

00:01:59,109 --> 00:01:57,710

signals limited what else can we do one

47

00:02:01,750 --> 00:01:59,119

of the things that people doing this is

48

00:02:03,789 --> 00:02:01,760

a little nice little paper of Aaron's is

49

00:02:05,620 --> 00:02:03,799

to look at modern stuff and say well

50

00:02:08,139 --> 00:02:05,630

some interesting analogies between

51
00:02:11,320 --> 00:02:08,149
modern biological systems and presumed

52
00:02:13,210 --> 00:02:11,330
ancient systems what we're trying to do

53
00:02:14,800 --> 00:02:13,220
is sort of say okay that's a great idea

54
00:02:18,280 --> 00:02:14,810
can we take that a little bit further

55
00:02:19,570 --> 00:02:18,290
and say do some experiments to try and

56
00:02:21,830 --> 00:02:19,580
retrace some of the steps towards

57
00:02:23,690 --> 00:02:21,840
evolution and modern systems but more

58
00:02:27,920 --> 00:02:23,700
biological perspective sort of coming

59
00:02:29,860 --> 00:02:27,930
top-down if you will so there's been a

60
00:02:33,800 --> 00:02:29,870
lot of really impressive high-tech

61
00:02:36,320 --> 00:02:33,810
presentations around methods I've seen

62
00:02:37,729 --> 00:02:36,330
some quite quite spectacular pieces of

63
00:02:40,250 --> 00:02:37,739

work and I just wanted to contribute our

64

00:02:43,880 --> 00:02:40,260

own high-tech approach to how we do this

65

00:02:45,880 --> 00:02:43,890

experiment so this is a school lunch box

66

00:02:48,740 --> 00:02:45,890

we used to pack in more and more

67

00:02:51,830 --> 00:02:48,750

multiple evolution experiments on top of

68

00:02:54,440 --> 00:02:51,840

one other so there you go there's all

69

00:02:56,150 --> 00:02:54,450

kinds of ways you can do astrobiology so

70

00:02:57,800 --> 00:02:56,160

some of the questions were trying to

71

00:03:00,470 --> 00:02:57,810

grapple with with our little lunch box

72

00:03:01,670 --> 00:03:00,480

setup are listed here and I don't have

73

00:03:03,860 --> 00:03:01,680

time to go through all of them but I

74

00:03:06,380 --> 00:03:03,870

will give you a brief overview so this

75

00:03:08,080 --> 00:03:06,390

one here instead of with understanding

76

00:03:10,160 --> 00:03:08,090

how bacterial translation initiation

77

00:03:12,170 --> 00:03:10,170

evolved and I'll talk about that one a

78

00:03:14,809 --> 00:03:12,180

little more this one I don't have time

79

00:03:16,580 --> 00:03:14,819

to talk about but I'm happy to talk to

80

00:03:18,470 --> 00:03:16,590

people about this so we've done a little

81

00:03:20,750 --> 00:03:18,480

experiment where we've applied a

82

00:03:24,289 --> 00:03:20,760

continual bottleneck to to see whether

83

00:03:26,930 --> 00:03:24,299

we get complex RNA processes and heavier

84

00:03:28,879 --> 00:03:26,940

check with that about that later on and

85

00:03:30,979 --> 00:03:28,889

then the final one is we're actually

86

00:03:32,930 --> 00:03:30,989

looking now at trying to understand how

87

00:03:35,300 --> 00:03:32,940

DNA might have evolved and I'll come

88

00:03:37,129 --> 00:03:35,310

back to that again at the end so for

89

00:03:39,410 --> 00:03:37,139

translation initiation one of the things

90

00:03:42,140 --> 00:03:39,420

that we we thought was puzzling as

91

00:03:44,599 --> 00:03:42,150

biologists is that bacteria use this

92

00:03:48,289 --> 00:03:44,609

formulation process so everybody charges

93

00:03:50,629 --> 00:03:48,299

their T RNAs so you get a charged tRNA

94

00:03:52,400 --> 00:03:50,639

so this is the initiator and then in

95

00:03:54,170 --> 00:03:52,410

bacteria you have a couple of extra

96

00:03:57,250 --> 00:03:54,180

steps that you don't find in our carrier

97

00:04:00,020 --> 00:03:57,260

you carrots the first one is edition of

98

00:04:02,240 --> 00:04:00,030

the Fulton group here through an enzyme

99

00:04:06,770 --> 00:04:02,250

called a formal transferase translation

100

00:04:09,229 --> 00:04:06,780

then proceeds but as the growing peptide

101

00:04:11,839 --> 00:04:09,239

comes out of the the ribosome exit so I

102

00:04:14,659 --> 00:04:11,849

another enzyme peptid formulae's comes

103

00:04:17,629 --> 00:04:14,669

along and what's that for mate group off

104

00:04:19,339 --> 00:04:17,639

again so this is before the proteins

105

00:04:21,110 --> 00:04:19,349

really had a chance to do anything so

106

00:04:23,930 --> 00:04:21,120

it's an odd thing that you add something

107

00:04:27,460 --> 00:04:23,940

and then remove it all prior to getting

108

00:04:29,810 --> 00:04:27,470

to a point of a functioning protein

109

00:04:32,600 --> 00:04:29,820

interestingly if you treat with a drug

110

00:04:34,850 --> 00:04:32,610

that knocks out production of

111

00:04:37,879 --> 00:04:34,860

this cofactor that's required for this

112

00:04:39,680 --> 00:04:37,889

reaction here you force cells to use the

113

00:04:44,360 --> 00:04:39,690

unmodified version here so a methanol

114

00:04:45,920 --> 00:04:44,370

tRNA you can also do knockouts which

115

00:04:47,719 --> 00:04:45,930

cells don't really like but they are

116

00:04:50,680 --> 00:04:47,729

viable where you eliminate both of these

117

00:04:53,029 --> 00:04:50,690

genes and you get the same thing

118

00:04:56,240 --> 00:04:53,039

proceeding in translation proceeding

119

00:04:59,960 --> 00:04:56,250

with a non modified version of society

120

00:05:02,600 --> 00:04:59,970

of confining and finally if we look

121

00:05:04,219 --> 00:05:02,610

across the Tree of Life this is a it's

122

00:05:06,020 --> 00:05:04,229

not a universal process you only see

123

00:05:09,350 --> 00:05:06,030

this in bacteria archaea and eukaryotes

124

00:05:11,230 --> 00:05:09,360

don't do this so we thought gee that

125

00:05:14,180 --> 00:05:11,240

looks a bit strange it sort of looks

126

00:05:15,860 --> 00:05:14,190

partly like it's not that important or

127

00:05:18,080 --> 00:05:15,870

necessary because only some parts of the

128

00:05:19,520 --> 00:05:18,090

tree use it and it's intriguing that you

129

00:05:21,800 --> 00:05:19,530

can knock something out that's being

130

00:05:24,469 --> 00:05:21,810

conserved within bacteria for possibly

131

00:05:26,839 --> 00:05:24,479

several billion years so we did an

132

00:05:29,689 --> 00:05:26,849

experiment to figure that out so what

133

00:05:32,990 --> 00:05:29,699

what Alanna rickety who's here and Ryan

134

00:05:34,760 --> 00:05:33,000

Catchpole did was to do a bunch of

135

00:05:36,189 --> 00:05:34,770

experiments and this is one of them here

136

00:05:40,580 --> 00:05:36,199

so what we're doing is we're evolving

137

00:05:42,140 --> 00:05:40,590

two lines over about 1500 generations so

138

00:05:44,719 --> 00:05:42,150

this blue line here is just a wild-type

139

00:05:46,550 --> 00:05:44,729

control and this gray one here is a

140

00:05:48,770 --> 00:05:46,560

knockout where we've eliminated both of

141

00:05:50,719 --> 00:05:48,780

those genes required for formulation and

142

00:05:52,459 --> 00:05:50,729

you can see that after about fifteen

143

00:05:56,029 --> 00:05:52,469

hundred generations their their growth

144

00:05:58,610 --> 00:05:56,039

is indistinguishable so it seems that

145

00:06:01,850 --> 00:05:58,620

you can be a bacterium quite happily

146

00:06:03,589 --> 00:06:01,860

without this process the thing that we

147

00:06:05,270 --> 00:06:03,599

thought was quite unusual about this is

148

00:06:07,580 --> 00:06:05,280

that the addition and removal looks a

149

00:06:09,110 --> 00:06:07,590

little bit like a toxin antitoxin system

150

00:06:10,610 --> 00:06:09,120

so I don't know if you guys are familiar

151

00:06:13,249 --> 00:06:10,620

with these idea they're sort of

152

00:06:14,510 --> 00:06:13,259

addiction systems so given what I know a

153

00:06:16,370 --> 00:06:14,520

lot of time I'll walk you through the

154

00:06:17,930 --> 00:06:16,380

experiment that we did to test this at

155

00:06:21,320 --> 00:06:17,940

the same time as explaining what they

156

00:06:23,029 --> 00:06:21,330

are so we think it's it this may this

157

00:06:25,490 --> 00:06:23,039

could have evolved originally virus

158

00:06:27,230 --> 00:06:25,500

elfish element so let's do this

159

00:06:30,950 --> 00:06:27,240

experiment here let's reintroduce those

160

00:06:34,040 --> 00:06:30,960

D D formulas informal formulas genes

161

00:06:35,330 --> 00:06:34,050

back into these evolved lines and so the

162

00:06:38,379 --> 00:06:35,340

way we do that is to put them onto a

163

00:06:41,390 --> 00:06:38,389

plasmid if you put a plasmid into a cell

164

00:06:44,980 --> 00:06:41,400

without any any kind of selection marker

165

00:06:46,780 --> 00:06:44,990

or whatever it will sometimes mistake

166

00:06:48,520 --> 00:06:46,790

and you can have individuals that lose

167

00:06:50,800 --> 00:06:48,530

the plasmid but they're not affected by

168

00:06:53,230 --> 00:06:50,810

that in our experiment what we've done

169

00:06:55,330 --> 00:06:53,240

is we forced the plasmid up by using a

170

00:06:57,220 --> 00:06:55,340

temperature sensitive one so we kick it

171

00:06:58,870 --> 00:06:57,230

out and what you see here is two

172

00:07:00,580 --> 00:06:58,880

different lines so these two one of

173

00:07:02,740 --> 00:07:00,590

these as colony forming units and the

174

00:07:04,810 --> 00:07:02,750

other is optical density so two ways of

175

00:07:07,240 --> 00:07:04,820

measuring growth and you can see this is

176

00:07:08,770 --> 00:07:07,250

the plasmid occupancy you can see the

177

00:07:10,900 --> 00:07:08,780

plasmid it gets kicked out pretty

178

00:07:14,200 --> 00:07:10,910

quickly but it has no effect on growth

179

00:07:16,420 --> 00:07:14,210

if we take a known toxin antitoxin

180

00:07:18,880 --> 00:07:16,430

system and do the same experiment so we

181

00:07:22,000 --> 00:07:18,890

take the exact same plasmid put a toxin

182

00:07:23,770 --> 00:07:22,010

antitoxin system on it and then force a

183

00:07:25,630 --> 00:07:23,780

kick out we get a very different curve

184

00:07:27,570 --> 00:07:25,640

here so there are two things that are

185

00:07:30,070 --> 00:07:27,580

that are happening here

186

00:07:32,230 --> 00:07:30,080

one is the plasmid is getting kicked out

187

00:07:35,320 --> 00:07:32,240

but the second is that both the

188

00:07:36,880 --> 00:07:35,330

measurements of growth are showing a

189

00:07:39,340 --> 00:07:36,890

reduction in growth and so what's

190

00:07:41,260 --> 00:07:39,350

happening in this system here is that

191

00:07:43,540 --> 00:07:41,270

when you get a knockout of the loss of

192

00:07:45,100 --> 00:07:43,550

the the plasmid you get cell this and

193

00:07:47,620 --> 00:07:45,110

this is sort of the cleverness of these

194

00:07:50,560 --> 00:07:47,630

addiction systems basically the way they

195

00:07:52,900 --> 00:07:50,570

work is if you get rid of one gene that

196

00:07:55,930 --> 00:07:52,910

is you're effectively your antidote to

197

00:07:58,150 --> 00:07:55,940

the toxin and both of these are carried

198

00:08:00,060 --> 00:07:58,160

here then you can no longer protect

199

00:08:03,930 --> 00:08:00,070

yourself against the toxin and you die

200

00:08:07,330 --> 00:08:03,940

so we did the same exact same experiment

201
00:08:08,890 --> 00:08:07,340
reintroducing our two genes the

202
00:08:12,010 --> 00:08:08,900
formulation the and the methyl

203
00:08:13,390 --> 00:08:12,020
transferase back on a plasmid and if we

204
00:08:15,100 --> 00:08:13,400
get this kind of result then we would

205
00:08:16,990 --> 00:08:15,110
say there's no sort of selfish element

206
00:08:20,350 --> 00:08:17,000
activity if we get this kind of result

207
00:08:22,480 --> 00:08:20,360
it would be consistent with this post

208
00:08:25,360 --> 00:08:22,490
segregation of killing phenotype

209
00:08:27,280 --> 00:08:25,370
and here's the result so we think that's

210
00:08:31,240 --> 00:08:27,290
pretty clear that once you've removed

211
00:08:33,460 --> 00:08:31,250
these two genes from this lineage and

212
00:08:35,290 --> 00:08:33,470
evolved them to sort of tolerate not

213
00:08:36,910 --> 00:08:35,300

having them and you put them back in you

214

00:08:41,460 --> 00:08:36,920

don't get sort of a complementation

215

00:08:44,410 --> 00:08:41,470

phenotype you get an addiction phenotype

216

00:08:46,330 --> 00:08:44,420

so what we think is is happening then is

217

00:08:47,620 --> 00:08:46,340

that these things are functional now and

218

00:08:49,270 --> 00:08:47,630

it's a you could I give everything's

219

00:08:51,670 --> 00:08:49,280

co-evolved you kind of need them because

220

00:08:53,620 --> 00:08:51,680

they're there but it's not obvious to us

221

00:08:55,180 --> 00:08:53,630

that this is particularly adaptive and

222

00:08:56,770 --> 00:08:55,190

there's two reasons for that one is we

223

00:08:58,420 --> 00:08:56,780

can get rid of it with no effect on

224

00:09:00,640 --> 00:08:58,430

growth after we

225

00:09:02,230 --> 00:09:00,650

sort of readapted that lineages the

226

00:09:05,079 --> 00:09:02,240

other two lineages are care and

227

00:09:06,700 --> 00:09:05,089

eukaryotes don't use this so it seems

228

00:09:08,500 --> 00:09:06,710

that this there may not be an adaptive

229

00:09:12,670 --> 00:09:08,510

function what we think might instead

230

00:09:16,540 --> 00:09:12,680

have happened is that this parasite got

231

00:09:18,130 --> 00:09:16,550

in and ensconced itself in translation

232

00:09:20,079 --> 00:09:18,140

and then the whole system is sort of

233

00:09:21,610 --> 00:09:20,089

co-evolved around that and once that's

234

00:09:23,050 --> 00:09:21,620

done that you can't actually get rid of

235

00:09:28,810 --> 00:09:23,060

it but not for reasons if it being

236

00:09:32,920 --> 00:09:28,820

advantageous okay so the second thing

237

00:09:37,450 --> 00:09:32,930

just how am I going for timer a little

238

00:09:39,850 --> 00:09:37,460

bit of time okay cool so I just used the

239

00:09:41,950 --> 00:09:39,860

last couple of slides just to tell you

240

00:09:44,829 --> 00:09:41,960

some stuff that's much earlier on in the

241

00:09:47,440 --> 00:09:44,839

process we're interested in this pathway

242

00:09:49,570 --> 00:09:47,450

here this shows how the DNA building

243

00:09:50,829 --> 00:09:49,580

blocks are made in all cells so

244

00:09:52,750 --> 00:09:50,839

basically what happens is you get the

245

00:09:55,360 --> 00:09:52,760

RNA building blocks here an enzyme

246

00:09:59,579 --> 00:09:55,370

called ribonucleotide reductase performs

247

00:10:02,320 --> 00:09:59,589

a reaction to convert these into deoxy

248

00:10:05,710 --> 00:10:02,330

ribose nucleotides but as you can see if

249

00:10:07,420 --> 00:10:05,720

you start from you your fourth deoxy is

250

00:10:11,920 --> 00:10:07,430

going to be a DLC you and there's a

251
00:10:15,850 --> 00:10:11,930
bolt-on pathway here to get to T so some

252
00:10:18,430 --> 00:10:15,860
of you may hopefully have seen a poster

253
00:10:21,579 --> 00:10:18,440
by Alana rickety but if you haven't

254
00:10:23,710 --> 00:10:21,589
please come take a look at it she's been

255
00:10:25,810 --> 00:10:23,720
addressing this these two questions here

256
00:10:27,970 --> 00:10:25,820
one can we delete these steps the answer

257
00:10:31,570 --> 00:10:27,980
is yes you can so she now has lines

258
00:10:35,079 --> 00:10:31,580
growing that don't do any of these steps

259
00:10:36,430 --> 00:10:35,089
here so they should stop at deoxy U and

260
00:10:40,570 --> 00:10:36,440
then what we've been doing is trying to

261
00:10:44,470 --> 00:10:40,580
get them to adapt to the absence of this

262
00:10:47,740 --> 00:10:44,480
pathway by supplementing them with the

263
00:10:50,380 --> 00:10:47,750

oxy T in the medium but then ratcheting

264

00:10:51,940 --> 00:10:50,390

down the amount that they have and so it

265

00:10:53,800 --> 00:10:51,950

still early days but she now has them

266

00:10:55,930 --> 00:10:53,810

growing without supplement whatsoever so

267

00:10:58,360 --> 00:10:55,940

our next question will be sort of what's

268

00:11:01,030 --> 00:10:58,370

happening there at the genome level is

269

00:11:03,310 --> 00:11:01,040

your asil accumulating we've also gone

270

00:11:04,510 --> 00:11:03,320

after arriving nucleotide reduction and

271

00:11:07,360 --> 00:11:04,520

I'll just show you some very preliminary

272

00:11:09,670 --> 00:11:07,370

results on that so question we we sort

273

00:11:11,800 --> 00:11:09,680

of had is can we eliminate this pathway

274

00:11:14,730 --> 00:11:11,810

turns out we can do a knock out of that

275

00:11:17,439 --> 00:11:14,740

and you have to supplement with the four

276

00:11:20,590 --> 00:11:17,449

deoxyribonucleotides for this cell line

277

00:11:22,300 --> 00:11:20,600

to survive so two people were being

278

00:11:24,329 --> 00:11:22,310

working on this analysis if I ever form

279

00:11:26,559 --> 00:11:24,339

an honor student and Sam heiress who's

280

00:11:28,179 --> 00:11:26,569

in the lab is the technician at the

281

00:11:30,160 --> 00:11:28,189

moment but it's probably more postdoc

282

00:11:32,139 --> 00:11:30,170

than a technician and what you can see

283

00:11:35,379 --> 00:11:32,149

is over about eight transfers that we've

284

00:11:37,090 --> 00:11:35,389

done so far we see a tenfold reduction

285

00:11:40,480 --> 00:11:37,100

in the dependency so this is sort of

286

00:11:42,759 --> 00:11:40,490

minimum concentration that these eco

287

00:11:43,990 --> 00:11:42,769

lice can survive on in terms of

288

00:11:46,179 --> 00:11:44,000

supplements so they're in a minimal

289

00:11:48,910 --> 00:11:46,189

media with a little bit of glucose and

290

00:11:51,400 --> 00:11:48,920

then a supplement of deoxyribonucleoside

291

00:11:52,990 --> 00:11:51,410

so they're clearly adapting to that this

292

00:11:55,660 --> 00:11:53,000

may be tricky to see but while here's

293

00:11:57,429 --> 00:11:55,670

some wild type e.coli and what we get is

294

00:12:00,249 --> 00:11:57,439

a very interesting sort of elongate

295

00:12:02,470 --> 00:12:00,259

stress morphology in these bacteria so

296

00:12:05,170 --> 00:12:02,480

this is a transfer one you can see that

297

00:12:07,269 --> 00:12:05,180

these Ecola much much longer than in the

298

00:12:10,119 --> 00:12:07,279

wild-type and some of these are you know

299

00:12:12,220 --> 00:12:10,129

ridiculously long by about transfer six

300

00:12:14,590 --> 00:12:12,230

other sort of some of them may be I

301
00:12:17,860 --> 00:12:14,600
think thirty to forty micrometers so

302
00:12:19,749 --> 00:12:17,870
they're huge not very heavy anyway so

303
00:12:21,009 --> 00:12:19,759
we're still working on that and of

304
00:12:23,199 --> 00:12:21,019
course one of the challenges is whether

305
00:12:27,120 --> 00:12:23,209
we we actually need to eliminate this

306
00:12:29,949 --> 00:12:27,130
before we we can get complete loss of

307
00:12:33,400 --> 00:12:29,959
dependency on this pathway here so I

308
00:12:34,540 --> 00:12:33,410
leave you with that teaser and just make

309
00:12:36,340 --> 00:12:34,550
some acknowledgments that are people to

310
00:12:37,870 --> 00:12:36,350
do the work and obviously if you ever

311
00:12:40,179 --> 00:12:37,880
want to do any research involving

312
00:12:42,309 --> 00:12:40,189
lunchboxes I can highly recommend this

313
00:12:43,600 --> 00:12:42,319

New Zealand company here that makes it's

314

00:13:16,180 --> 00:12:43,610

probably the world's best Google lunch

315

00:13:16,190 --> 00:13:30,389

[Music]

316

00:13:34,930 --> 00:13:33,150

yeah I mean we've done a bunch of other

317

00:13:36,400 --> 00:13:34,940

experiments which I didn't have time to

318

00:13:38,259 --> 00:13:36,410

present but you know we've knocked them

319

00:13:39,699 --> 00:13:38,269

into the genome and looked at whether

320

00:13:42,910 --> 00:13:39,709

there's a fitness improvement there

321

00:13:44,530 --> 00:13:42,920

isn't we we noticed that they become

322

00:13:48,939 --> 00:13:44,540

very very difficult to knock out as soon

323

00:13:51,400 --> 00:13:48,949

as you've got them in we yes we've also

324

00:13:52,120 --> 00:13:51,410

sort of evolved the the knock in lines

325

00:13:54,430 --> 00:13:52,130

again

326

00:13:56,530 --> 00:13:54,440

to see whether the system rear depth and

327

00:13:59,620 --> 00:13:56,540

it becomes very difficult to remove them

328

00:14:06,309 --> 00:13:59,630

and we definitely see that so this is a

329

00:14:08,650 --> 00:14:06,319

bunch of other data for sure okay thank

330

00:14:10,020 --> 00:14:08,660

you and so we have to move to our next

331

00:14:12,490 --> 00:14:10,030

speaker sync thanks again