# AbSciCon 2019

1
00:00:00,790 --> 00:00:07,320
[Music]

2
00:00:12,390 --> 00:00:09,060
[Applause]

3
00:00:16,299 --> 00:00:12,400
good afternoon everyone this is a very

4
00:00:19,600 --> 00:00:16,309
aggressive AK with the other theories

5
00:00:21,429 --> 00:00:19,610
about ribosome evolution so I'm Jessica

6
00:00:23,670 --> 00:00:21,439
Bowman I work in Lauren Williams lab at

7
00:00:26,290 --> 00:00:23,680
Georgia Tech I'm part of the cool Center

8
00:00:28,959 --> 00:00:26,300
you might recognize this picture from a

9
00:00:31,450 --> 00:00:28,969
few minutes ago so what I'm going to

10
00:00:35,410 --> 00:00:31,460
talk to you today about is excavating

11
00:00:39,400 --> 00:00:35,420
the root of the tree of life this is a

12
00:01:01,690 --> 00:00:39,410
tree of life which is Jillian Banfield's

13
00:01:08,630 --> 00:01:05,240

so this is Gillian Banfield's new tree

14
00:01:10,219 --> 00:01:08,640
of life this is based on the 16

15
00:01:12,500 --> 00:01:10,229
different ribosomal protein sequences

16
00:01:14,240 --> 00:01:12,510
consensus of these you can see there's a

17
00:01:16,400 --> 00:01:14,250
lot of diversity here in bacteria we

18
00:01:18,109 --> 00:01:16,410
also have a lot of diversity or we're

19
00:01:21,770 --> 00:01:18,119
not quite as much in archaea and Eukarya

20
00:01:23,060 --> 00:01:21,780
and if we arbitrarily place Luca here so

21
00:01:25,010 --> 00:01:23,070
we're not rooting the Tree of Life we're

22
00:01:26,990 --> 00:01:25,020
just arbitrarily placing Luca here what

23
00:01:29,240 --> 00:01:27,000
we can do is look back and see if we can

24
00:01:31,940 --> 00:01:29,250
excavate this Tree of Life and ask the

25
00:01:33,740 --> 00:01:31,950
question whether the diversity of modern

26
00:01:36,530 --> 00:01:33,750
life what the diversity of modern life

27
00:01:41,180 --> 00:01:36,540
tells us about the evolution of biology

28
00:01:43,249 --> 00:01:41,190
before Luca so as many of you know this

29
00:01:44,960 --> 00:01:43,259
is the the ribosome we have a large

30
00:01:46,550 --> 00:01:44,970
subunit we have a small subunit the

31
00:01:50,030 --> 00:01:46,560
small subunit is responsible for

32
00:01:52,279 --> 00:01:50,040
decoding the large subunit contains the

33
00:01:54,139 --> 00:01:52,289
peptidyl transferase center which is the

34
00:01:56,810 --> 00:01:54,149
region of the ribosome in which the

35
00:01:58,039 --> 00:01:56,820
amino acyl Aidid trna transfers the

36
00:02:02,330 --> 00:01:58,049
amino acid to the growing polypeptide

37
00:02:04,700 --> 00:02:02,340
chain this is a ribosome structure by a

38
00:02:07,100 --> 00:02:04,710

hairy Nola's group we have the small

39
00:02:10,759 --> 00:02:07,110
subunit ribosomal RNA in blue the large

40
00:02:14,539 --> 00:02:10,769
subunit in gray there is a red tRNA here

41
00:02:16,009 --> 00:02:14,549
and the this is the piece art tRNA we

42
00:02:17,150 --> 00:02:16,019
know because there's an alpha helical

43
00:02:19,970 --> 00:02:17,160
structure of the growing polypeptide

44
00:02:22,789 --> 00:02:19,980
chain extending through this long exit

45
00:02:25,280 --> 00:02:22,799
tunnel and so the the useful thing for

46
00:02:26,810 --> 00:02:25,290
us is that we now have many different

47
00:02:28,729 --> 00:02:26,820
ribosome structures so we have ribosomes

48
00:02:31,280 --> 00:02:28,739
from all three trees of life to all

49
00:02:34,009 --> 00:02:31,290
three major branches and then some

50
00:02:35,660 --> 00:02:34,019
either crystal structures or cryo-em

51
00:02:40,190 --> 00:02:35,670
structures in the case of some of the

52
00:02:42,920 --> 00:02:40,200
more advanced eukaryotes so if we look

53
00:02:44,360 --> 00:02:42,930
at the e coli structure of ribosomal RNA

54
00:02:46,069 --> 00:02:44,370
this is a piece from the large subunit

55
00:02:50,030 --> 00:02:46,079
near the peptidyl transferase center

56
00:02:52,310 --> 00:02:50,040
what we can see is that we have a an RNA

57
00:02:56,240 --> 00:02:52,320
backbone here indicated in red this is

58
00:02:58,910 --> 00:02:56,250
of E coli bacteria we've superimposed

59
00:03:00,920 --> 00:02:58,920
this with a halo our Keela marichuy

60
00:03:03,979 --> 00:03:00,930
represented in our cans so from another

61
00:03:05,500 --> 00:03:03,989
domain of life and superimposed this

62
00:03:08,559 --> 00:03:05,510
with a yeast

63
00:03:12,400 --> 00:03:08,569

from the Eukarya and then with Homo

64
00:03:15,280 --> 00:03:12,410
sapiens and mitochondrial ribosomal RNA

65
00:03:17,949 --> 00:03:15,290
the same region of the large subunit

66
00:03:20,770 --> 00:03:17,959
what we see is that over 3.8 to 4

67
00:03:24,940 --> 00:03:20,780
billion years this ribosome really has

68
00:03:27,309 --> 00:03:24,950
not changed which is kind of amazing we

69
00:03:31,240 --> 00:03:27,319
can found this the boundaries of this

70
00:03:33,070 --> 00:03:31,250
conservation this conserved core as we

71
00:03:36,160 --> 00:03:33,080
call it we can resolve these boundaries

72
00:03:39,009 --> 00:03:36,170
within the ribosome with ribosomes of E

73
00:03:41,650 --> 00:03:39,019
coli of private caucus furiosa's which

74
00:03:43,930 --> 00:03:41,660
is another archaea and also within yeast

75
00:03:46,120 --> 00:03:43,940
down here we have the small subunit

76
00:03:49,180 --> 00:03:46,130
shown on the left the large subunit on

77
00:03:51,610 --> 00:03:49,190
the right the blue represents the common

78
00:03:53,920 --> 00:03:51,620
core of the ribosomal RNA for the large

79
00:03:56,620 --> 00:03:53,930
subunit the red here represents the

80
00:03:59,410 --> 00:03:56,630
common core of the small subunit if you

81
00:04:02,920 --> 00:03:59,420
notice if you look down this slide you

82
00:04:05,680 --> 00:04:02,930
begin to see that the gray portion which

83
00:04:08,319 --> 00:04:05,690
is the non common core or the RNA that's

84
00:04:10,390 --> 00:04:08,329
specific to that species seems to be

85
00:04:14,080 --> 00:04:10,400
increasing in proportion to the total

86
00:04:16,840 --> 00:04:14,090
amount of RNA and you would be right in

87
00:04:20,740 --> 00:04:16,850
that if you look at homosapiens

88
00:04:22,840 --> 00:04:20,750

ribosomal RNA you can see here this is

89
00:04:24,730 --> 00:04:22,850
the secondary structure in gray is what

90
00:04:27,190 --> 00:04:24,740
we call the common core and green these

91
00:04:28,990 --> 00:04:27,200
are expansion segments so the pieces of

92
00:04:31,990 --> 00:04:29,000
RNA that protrude beyond that common

93
00:04:33,520 --> 00:04:32,000
core and in pink here is one expansion

94
00:04:38,469 --> 00:04:33,530
segment in particular that I'm going to

95
00:04:40,659 --> 00:04:38,479
highlight so this is what we call es7 if

96
00:04:43,960 --> 00:04:40,669
we look at these expansion segments

97
00:04:46,510 --> 00:04:43,970
relative to the diameter of the sphere

98
00:04:48,279 --> 00:04:46,520
this common core and then what we call

99
00:04:50,409 --> 00:04:48,289
the eukaryotic shell that so the

100
00:04:53,320 --> 00:04:50,419
expansions beyond that common core

101
00:04:56,379 --> 00:04:53,330
that's universal to all organisms we see

102
00:04:58,990 --> 00:04:56,389
that these expansion segments especially

103
00:05:03,159 --> 00:04:59,000
expansion segments 7 and 27 of the human

104
00:05:06,040 --> 00:05:03,169
ribosome extend quite a long ways if we

105
00:05:08,890 --> 00:05:06,050
follow this expansion segment 7 which

106
00:05:11,800 --> 00:05:08,900
actually begins as a helix 25 in the

107
00:05:16,930 --> 00:05:11,810
e.coli ribosome you notice if we go to

108
00:05:19,300 --> 00:05:16,940
yeast here this purple is this helix 25

109
00:05:23,380 --> 00:05:19,310
it's growing as we then move and

110
00:05:25,120 --> 00:05:23,390
fruit fly and then into Homo sapiens if

111
00:05:26,680 --> 00:05:25,130
we look at this in three dimensions and

112
00:05:27,780 --> 00:05:26,690
someone emphasized earlier the

113
00:05:29,770 --> 00:05:27,790

importance of looking at

114
00:05:31,930 --> 00:05:29,780
three-dimensional structures instead of

115
00:05:34,930 --> 00:05:31,940
just sequences or two dimensional

116
00:05:36,790 --> 00:05:34,940
structures we see helix 25 this is from

117
00:05:39,430 --> 00:05:36,800
the e.coli the bacteria we can

118
00:05:41,290 --> 00:05:39,440
superimpose that with the crystal

119
00:05:43,750 --> 00:05:41,300
structure data of the archaea or the

120
00:05:46,690 --> 00:05:43,760
halo are Kili keyless Marist more dream

121
00:05:48,630 --> 00:05:46,700
and what we see is that the there

122
00:05:52,750 --> 00:05:48,640
appears to be a common ancestor of

123
00:05:54,970 --> 00:05:52,760
archaea in bacteria possibly we can a

124
00:05:58,960 --> 00:05:54,980
superimpose the archaea with yeast and

125
00:06:01,180 --> 00:05:58,970
see that the the ancestor of the yeast

126
00:06:04,300 --> 00:06:01,190
ribosomal RNA seems to be best

127
00:06:08,320 --> 00:06:04,310
approximated by an arcane and we can

128
00:06:11,640 --> 00:06:08,330
continue on with fruit fly and up to

129
00:06:14,170 --> 00:06:11,650
human this is quite a substantial

130
00:06:18,160 --> 00:06:14,180
elaboration on this three-dimensional

131
00:06:25,470 --> 00:06:18,170
structure to have begun with a helix

132
00:06:29,260 --> 00:06:25,480
that is conserved in bacterial today so

133
00:06:31,270 --> 00:06:29,270
what can this comparison of modern

134
00:06:32,920 --> 00:06:31,280
organisms tell us about the ribosome

135
00:06:35,830 --> 00:06:32,930
before the last Universal common

136
00:06:38,200 --> 00:06:35,840
ancestor so if we look closely at each

137
00:06:39,670 --> 00:06:38,210
of these sites of expansion in each of

138
00:06:42,130 --> 00:06:39,680

these expansion segments we see that

139
00:06:44,980 --> 00:06:42,140
there is a unique geometric fingerprint

140
00:06:47,110 --> 00:06:44,990
and most of them which we call an

141
00:06:49,920 --> 00:06:47,120
insertion site if you notice these two

142
00:06:51,880 --> 00:06:49,930
believe this is archaea and e-coli

143
00:06:54,010 --> 00:06:51,890
superimposed and this would be the

144
00:06:56,920 --> 00:06:54,020
eukaryotic expansion so this is kind of

145
00:06:58,300 --> 00:06:56,930
like the tree the trunk of a tree and a

146
00:07:00,490 --> 00:06:58,310
branch growing out of the tree

147
00:07:03,610 --> 00:07:00,500
so this ribosomal RNA grows without

148
00:07:06,610 --> 00:07:03,620
perturbing the common core this is helix

149
00:07:08,170 --> 00:07:06,620
52 so this is a portion of the ribosomal

150
00:07:10,210 --> 00:07:08,180
RNA that is different from the one I

151
00:07:12,490 --> 00:07:10,220
just told you showed you and this is

152
00:07:16,780 --> 00:07:12,500
helix 38 which is an entirely different

153
00:07:19,090 --> 00:07:16,790
expansion segment so we can make two

154
00:07:22,060 --> 00:07:19,100
observations one is that the modern

155
00:07:24,970 --> 00:07:22,070
ribosome post lucre grew and is growing

156
00:07:26,410 --> 00:07:24,980
by accretion and that the modern the

157
00:07:29,950 --> 00:07:26,420
second observation is that the modern

158
00:07:32,280 --> 00:07:29,960
ribosome post luca left some

159
00:07:34,620 --> 00:07:32,290
recognizable molecular finger

160
00:07:36,660 --> 00:07:34,630
so if we then combine those two with

161
00:07:40,320 --> 00:07:36,670
assumptions that the common core also

162
00:07:43,170 --> 00:07:40,330
grew by accretion and in the common core

163
00:07:45,090 --> 00:07:43,180

also left and in the common core

164
00:07:48,030 --> 00:07:45,100
these growth events or fingerprints were

165
00:07:50,280 --> 00:07:48,040
also left and we can go in and look at

166
00:07:52,440 --> 00:07:50,290
the common core of the ribosome for

167
00:07:55,290 --> 00:07:52,450
these insertion events and actually see

168
00:07:58,140 --> 00:07:55,300
back beyond the emergence of the last

169
00:08:00,740 --> 00:07:58,150
Universal common ancestor this is a

170
00:08:04,410 --> 00:08:00,750
model and it gives us a testable model

171
00:08:06,210 --> 00:08:04,420
so this is the superimposed helix 24 so

172
00:08:08,430 --> 00:08:06,220
this is actually in what we call the

173
00:08:10,500 --> 00:08:08,440
common core the ancestral expansion and

174
00:08:12,990 --> 00:08:10,510
here is a branch of ribosomal RNA coming

175
00:08:16,440 --> 00:08:13,000
out so this would be some kind of

176
00:08:18,660 --> 00:08:16,450
progression and the Luca R before Luca

177
00:08:25,890 --> 00:08:18,670
and we also see this type of insertion

178
00:08:28,710 --> 00:08:25,900
site in tRNA amazingly so this figure up

179
00:08:31,740 --> 00:08:28,720
here is entirely attributable to Anton

180
00:08:33,900 --> 00:08:31,750
Petrov in the back as this most of this

181
00:08:35,430 --> 00:08:33,910
presentation but if we look back to this

182
00:08:37,530 --> 00:08:35,440
common core and this is the common core

183
00:08:41,190 --> 00:08:37,540
of the large subunit here we can

184
00:08:44,100 --> 00:08:41,200
actually find these insertion sites all

185
00:08:46,020 --> 00:08:44,110
through the ribosome through the large

186
00:08:48,810 --> 00:08:46,030
subunit and each of these color

187
00:08:50,970 --> 00:08:48,820
transitions demarcates in a different

188
00:08:54,330 --> 00:08:50,980

insertion event in the last Universal

189
00:08:56,700 --> 00:08:54,340
common ancestor and these can be

190
00:08:59,750 --> 00:08:56,710
integrated through a progression over

191
00:09:02,640 --> 00:08:59,760
time and to generate phases possible a

192
00:09:06,420 --> 00:09:02,650
model of phases of like large subunit

193
00:09:07,980 --> 00:09:06,430
growth in which we have this phase one

194
00:09:09,960 --> 00:09:07,990
and phase two a dark blue and light blue

195
00:09:13,170 --> 00:09:09,970
this would be the peptidyl transferase

196
00:09:19,710 --> 00:09:15,450
one thing that wanted to emphasize is

197
00:09:22,260 --> 00:09:19,720
the effect of this model on the exit

198
00:09:25,290 --> 00:09:22,270
tunnel and the I guess the progression

199
00:09:27,600 --> 00:09:25,300
or folding or the the learning that

200
00:09:29,850 --> 00:09:27,610
proteins had to go through to fold at

201
00:09:32,370 --> 00:09:29,860
some point during evolution so this is

202
00:09:35,820 --> 00:09:32,380
the ribosome tRNA here in blue we have a

203
00:09:38,880 --> 00:09:35,830
growing peptide moving through the exit

204
00:09:41,760 --> 00:09:38,890
tunnel if we look at just the phase one

205
00:09:43,380 --> 00:09:41,770
so what we think is the oldest part of

206
00:09:44,400 --> 00:09:43,390
the large subunit and which is shown

207
00:09:47,579 --> 00:09:44,410
here

208
00:09:50,460 --> 00:09:47,589
and we progress through time consistent

209
00:09:52,999 --> 00:09:50,470
with our accretion model we add face to

210
00:09:55,470 --> 00:09:53,009
ribosomal RNA this develops an exit pore

211
00:09:58,980 --> 00:09:55,480
which would be this just the beginnings

212
00:10:02,490 --> 00:09:58,990
of this exit tunnel we add phase 3 phase

213
00:10:05,309 --> 00:10:02,500

4 phase five and faves six what we see

214
00:10:08,309 --> 00:10:05,319
is that the the most significant impact

215
00:10:10,590 --> 00:10:08,319
of this the phases and evolution of this

216
00:10:12,540 --> 00:10:10,600
in this model had to do with the

217
00:10:17,730 --> 00:10:12,550
elaboration and extension of the exit

218
00:10:20,639 --> 00:10:17,740
tunnel so there's a another person on

219
00:10:23,670 --> 00:10:20,649
our group Nick Kovacs who looked at

220
00:10:26,670 --> 00:10:23,680
protein folding over the different

221
00:10:28,559 --> 00:10:26,680
phases of the ribosome and found that

222
00:10:30,749 --> 00:10:28,569
the proteins that we don't have any

223
00:10:33,840 --> 00:10:30,759
ribosomal proteins in phase one but or

224
00:10:35,369 --> 00:10:33,850
two but in phase three the the proteins

225
00:10:37,740 --> 00:10:35,379
in Phase three are really characterized

226
00:10:39,360 --> 00:10:37,750
by these random coils and so this is

227
00:10:41,280 --> 00:10:39,370
unstructured protein and this has been

228
00:10:44,280 --> 00:10:41,290
shown by another graduate student from

229
00:10:45,929 --> 00:10:44,290
our group Katherine linear and then

230
00:10:48,389 --> 00:10:45,939
phase four we start to have some of

231
00:10:51,929 --> 00:10:48,399
these beta hairpins and then in Phase

232
00:10:53,460 --> 00:10:51,939
five we have more complex folds with

233
00:10:57,889 --> 00:10:53,470
these beta hairpins and some alpha

234
00:11:00,410 --> 00:10:57,899
helixes and so what we think is that the

235
00:11:02,910 --> 00:11:00,420
evolution of protein folding is

236
00:11:05,569 --> 00:11:02,920
concerted with the evolution of the exit

237
00:11:10,230 --> 00:11:05,579
tunnel I actually need to credit Moran

238
00:11:13,439 --> 00:11:10,240

sprinkle pinter with some interesting

239
00:11:16,889 --> 00:11:13,449
insights into this so what we think is

240
00:11:18,990 --> 00:11:16,899
that when the ribosomal RNA was in the

241
00:11:22,379 --> 00:11:19,000
early phases so it had only an exit pore

242
00:11:25,620 --> 00:11:22,389
no exit tunnel that in Phase three would

243
00:11:28,470 --> 00:11:25,630
have emerged random coral head times and

244
00:11:32,970 --> 00:11:28,480
as this exit tunnel became longer and

245
00:11:36,030 --> 00:11:32,980
longer we were able to accommodate these

246
00:11:38,610 --> 00:11:36,040
more advanced proteins so the idea is

247
00:11:40,710 --> 00:11:38,620
that when the exit tunnel is too short

248
00:11:43,590 --> 00:11:40,720
we de the formation of beta structures

249
00:11:46,170 --> 00:11:43,600
so we there's more likely to be

250
00:11:47,970 --> 00:11:46,180
aggregation that sort of thing so my

251
00:11:49,980 --> 00:11:47,980
conclusions today or that ribosomes

252
00:11:52,290 --> 00:11:49,990
evolved by chrétien of and without

253
00:11:54,509 --> 00:11:52,300
perturbation of four billion year old

254
00:11:56,819 --> 00:11:54,519
common core and that the evolution of

255
00:11:57,750 --> 00:11:56,829
the tunnel and protein folding were

256
00:12:01,710 --> 00:11:57,760
likely coupled

257
00:12:04,259 --> 00:12:01,720
I'd like to thank my group at Georgia

258
00:12:07,800 --> 00:12:04,269
Tech especially Lauren Williams the cool

259
00:12:09,900 --> 00:12:07,810
Center and our sponsors NASA and NSF and

260
00:12:12,540 --> 00:12:09,910
here is Anton our very important person

261
00:12:18,449 --> 00:12:12,550
in this work and also Nick Kovacs is

262
00:12:20,430 --> 00:12:18,459
here and moran and also peter was here

263
00:12:20,750 --> 00:12:20,440

right here all right thank you very much

264
00:12:25,699 --> 00:12:20,760
[Applause]

265
00:12:25,709 --> 00:12:43,189
we have time for a couple of questions

266
00:12:49,019 --> 00:12:47,490
destructor Southland and human I think

267
00:12:51,449 --> 00:12:49,029
at the time of Drosophila we probably

268
00:12:52,949 --> 00:12:51,459
would have had the more complex protein

269
00:12:56,939 --> 00:12:52,959
structures so the exit tunnel would have

270
00:12:59,460 --> 00:12:56,949
been closer to what we have today the

271
00:13:02,900 --> 00:12:59,470
address your question

272
00:13:09,260 --> 00:13:02,910
I just want to mention what they change

273
00:13:15,630 --> 00:13:14,010
something beyond the ribosome let me

274
00:13:17,430 --> 00:13:15,640
just comment on that the ribosomes

275
00:13:19,560 --> 00:13:17,440
throughout the three domains have all

276
00:13:21,870 --> 00:13:19,570
these kinds of weirds in insertions and

277
00:13:24,060 --> 00:13:21,880
deletions we do not know the functional

278
00:13:37,120 --> 00:13:24,070
aspects of those additions and deletions

279
00:13:40,480 --> 00:13:38,860
great it was really interesting one of

280
00:13:42,550 --> 00:13:40,490
the peculiar aspects of The Tree of Life

281
00:13:46,030 --> 00:13:42,560
is that there's these really long empty

282
00:13:49,420 --> 00:13:46,040
branches right and so your model seems

283
00:13:51,579 --> 00:13:49,430
to just suggest and I'm not saying it's

284
00:13:53,800 --> 00:13:51,589
not accurate but seems to suggest that

285
00:13:57,610 --> 00:13:53,810
somehow the bacteria the bacterial

286
00:14:01,060 --> 00:13:57,620
ribosome sort of stayed constant right

287
00:14:03,120 --> 00:14:01,070
and could form the node upon which the

288
00:14:06,070 --> 00:14:03,130

rest of the long you know the for the

289
00:14:08,050 --> 00:14:06,080
eukaryotes in archaea which you know it

290
00:14:11,620 --> 00:14:08,060
could be but that does require a lot of

291
00:14:13,269 --> 00:14:11,630
stasis for that bacterial ribosome which

292
00:14:16,150 --> 00:14:13,279
isn't reflected in the rest of the

293
00:14:18,250 --> 00:14:16,160
phylogeny yes I I don't know if you

294
00:14:19,780 --> 00:14:18,260
noticed but even in our bacterial model

295
00:14:22,930 --> 00:14:19,790
there's there's kind of a common even

296
00:14:25,480 --> 00:14:22,940
even though the e.coli structure

297
00:14:26,620 --> 00:14:25,490
ribosomal RNA is is approximates what we

298
00:14:30,579 --> 00:14:26,630
think is the common core they're not

299
00:14:32,949 --> 00:14:30,589
exactly the same so I think the that you

300
00:14:34,750 --> 00:14:32,959
coli may be a good approximation of an

301
00:14:36,370 --> 00:14:34,760
ancestral ribosome but is not

302
00:14:38,860 --> 00:14:36,380
necessarily something that was fixed in

303
00:14:44,079 --> 00:14:38,870
time in which eukaryotic ribosomes grew

304
00:14:45,250 --> 00:14:44,089
upon yeah you can speak to her after the

305
00:14:48,550 --> 00:14:45,260
segment because we are already running