# Glycosylation of Model Proto-RNA Nucleobases

Dr. David Fialho

Georgia Tech Astrobiology

1
00:00:12,650 --> 00:00:10,580
I really want to thank the organizers

2
00:00:14,720 --> 00:00:12,660
for giving me this opportunity to come

3
00:00:16,760 --> 00:00:14,730
talk so thank you very much as Moran

4
00:00:18,349 --> 00:00:16,770
said I look at the origin of life from

5
00:00:21,640 --> 00:00:18,359
the perspective of a physical organic

6
00:00:24,800 --> 00:00:21,650
chemist and from that perspective RNA

7
00:00:26,689 --> 00:00:24,810
it's something really tough to crack and

8
00:00:27,259 --> 00:00:26,699
I'm gonna give you insight into that

9
00:00:30,140 --> 00:00:27,269
right now

10
00:00:32,179 --> 00:00:30,150
so we all know about the RNA world

11
00:00:34,580 --> 00:00:32,189
hypothesis this research paradigm that

12
00:00:37,330 --> 00:00:34,590
says the DNA protein based biochemistry

13
00:00:41,209 --> 00:00:37,340

of extant life was preceded by a

14
00:00:44,240 --> 00:00:41,219
biochemistry predominantly mediated by

15
00:00:46,880 --> 00:00:44,250
RNA but there are serious problems with

16
00:00:50,690 --> 00:00:46,890
this if you're talking about a prebiotic

17
00:00:52,279 --> 00:00:50,700
root to RNA so I'm gonna show this

18
00:00:55,700 --> 00:00:52,289
approach which I've called a historical

19
00:00:57,439 --> 00:00:55,710
approach to RNA previously it was

20
00:00:59,660 --> 00:00:57,449
thought that we could start with simple

21
00:01:02,299 --> 00:00:59,670
prebiotic precursors and build them up

22
00:01:04,690 --> 00:01:02,309
incrementally to form RNA but there are

23
00:01:07,969 --> 00:01:04,700
many problems associated with this

24
00:01:11,390 --> 00:01:07,979
build-up approach for example we want

25
00:01:13,460 --> 00:01:11,400
the sugar ribose in RNA but ribose is

26
00:01:15,289 --> 00:01:13,470
produced among a variety of sugars in

27
00:01:16,760 --> 00:01:15,299
model prebiotic reactions so it's not

28
00:01:19,999 --> 00:01:16,770
immediately obvious how you would select

29
00:01:21,980 --> 00:01:20,009
ribose over other sugars furthermore

30
00:01:24,200 --> 00:01:21,990
even if you could get ribose the

31
00:01:26,030 --> 00:01:24,210
glycosylation chemistry required to make

32
00:01:27,710 --> 00:01:26,040
nucleus size does not work under

33
00:01:30,590 --> 00:01:27,720
periodically plausible conditions so

34
00:01:32,090 --> 00:01:30,600
here you see cytosine it does not form

35
00:01:33,940 --> 00:01:32,100
nucleus sites with ribose under

36
00:01:36,050 --> 00:01:33,950
periodically plausible conditions

37
00:01:38,749 --> 00:01:36,060
furthermore even if you could get this

38
00:01:40,609 --> 00:01:38,759

nucleus I'd there are problems

39
00:01:42,679 --> 00:01:40,619
associated with phosphorylation although

40
00:01:45,800 --> 00:01:42,689
we just saw beautiful beautiful work by

41
00:01:47,660 --> 00:01:45,810
Brad Libra car in my lab about a method

42
00:01:49,609 --> 00:01:47,670
to get over that nevertheless there are

43
00:01:54,200 --> 00:01:49,619
still problems about polymerization of

44
00:01:55,609 --> 00:01:54,210
those nucleotides to form RNA so in the

45
00:01:59,600 --> 00:01:55,619
HUD lab we take a different approach

46
00:02:01,249 --> 00:01:59,610
this approach postulates that RNA is the

47
00:02:04,039 --> 00:02:01,259
product of chemical or biological

48
00:02:05,749 --> 00:02:04,049
evolution and I don't think that this is

49
00:02:08,529 --> 00:02:05,759
too hard to accept if you're willing to

50
00:02:12,470 --> 00:02:08,539
accept the idea that DNA could have been

51
00:02:13,550 --> 00:02:12,480
the evolutionary product of RNA so DNA

52
00:02:15,290 --> 00:02:13,560
and RNA

53
00:02:18,199 --> 00:02:15,300
are the ones that exist today if

54
00:02:21,170 --> 00:02:18,209
something existed before that it has no

55
00:02:22,699 --> 00:02:21,180
evidence left over and it's a real tough

56
00:02:24,350 --> 00:02:22,709
challenge to figure out what the

57
00:02:26,180 --> 00:02:24,360
different components could have been so

58
00:02:27,979 --> 00:02:26,190
conceptually we start out by saying

59
00:02:31,400 --> 00:02:27,989
we're going to divide our proto nucleic

60
00:02:33,170 --> 00:02:31,410
acid into three distinct functional

61
00:02:35,030 --> 00:02:33,180
units the recognition unit which today

62
00:02:37,070 --> 00:02:35,040
are the nucleobases the tri functional

63
00:02:39,890 --> 00:02:37,080

connector which today is ribose or

64
00:02:42,589 --> 00:02:39,900
deoxyribose and the ionized linker which

65
00:02:44,390 --> 00:02:42,599
is phosphate today so then we're just

66
00:02:45,920 --> 00:02:44,400
going to go through each one and think

67
00:02:48,920 --> 00:02:45,930
about what are the most prebiotic lea

68
00:02:50,870 --> 00:02:48,930
reasonable precursors that we could have

69
00:02:53,240 --> 00:02:50,880
had so first we'll start with the

70
00:02:55,250 --> 00:02:53,250
recognition units in a prebiotic lea

71
00:02:57,650 --> 00:02:55,260
plausible mixture you would not just

72
00:02:59,420 --> 00:02:57,660
have au GNC but a variety of

73
00:03:01,370 --> 00:02:59,430
heterocyclic compounds that could have

74
00:03:03,589 --> 00:03:01,380
supported base pairing and could have

75
00:03:06,170 --> 00:03:03,599
been present in your proto RNA so how do

76
00:03:09,620 --> 00:03:06,180
we select certain ones from that to get

77
00:03:11,449 --> 00:03:09,630
to our candidate proto RNA the trick is

78
00:03:13,670 --> 00:03:11,459
that some of them have the ability to

79
00:03:16,280 --> 00:03:13,680
self sort out of this complex mixture

80
00:03:18,440 --> 00:03:16,290
and form super molecular assemblies so

81
00:03:20,240 --> 00:03:18,450
for example I have highlighted here try

82
00:03:23,449 --> 00:03:20,250
me know primitive in green and cyanuric

83
00:03:24,949 --> 00:03:23,459
acid in purple these are the ones among

84
00:03:27,140 --> 00:03:24,959
others that have the ability to self

85
00:03:29,120 --> 00:03:27,150
assemble if we can get this non covalent

86
00:03:30,710 --> 00:03:29,130
super molecular assembly perhaps we can

87
00:03:32,900 --> 00:03:30,720
use it as a scaffold to stitch together

88
00:03:37,220 --> 00:03:32,910

a polymer and create a true

89
00:03:38,809 --> 00:03:37,230
informational molecule now there are

90
00:03:40,580 --> 00:03:38,819
only certain heterocycles that will

91
00:03:42,470 --> 00:03:40,590
support a super molecular assembly such

92
00:03:44,150 --> 00:03:42,480
as these and these for the ones that

93
00:03:47,090 --> 00:03:44,160
were most interested in barbar Turek

94
00:03:49,970 --> 00:03:47,100
acid tap try muna prim adine cyanuric

95
00:03:53,000 --> 00:03:49,980
acid and melamine they formed this

96
00:03:55,280 --> 00:03:53,010
hexameric structure this hex ad which

97
00:03:57,979 --> 00:03:55,290
presents a very large stacking surface

98
00:04:00,650 --> 00:03:57,989
in water and because of that this

99
00:04:01,280 --> 00:04:00,660
hydrophobic surface allows them to stack

100
00:04:03,770 --> 00:04:01,290
on each other

101
00:04:05,780 --> 00:04:03,780
so that you hide most of the hydrophobic

102
00:04:10,039 --> 00:04:05,790
surface and you get this super molecular

103
00:04:11,599 --> 00:04:10,049
assembly in addition to that these

104
00:04:13,190 --> 00:04:11,609
heterocycles have the advantage that

105
00:04:16,430 --> 00:04:13,200
they are very chemically reactive

106
00:04:17,629 --> 00:04:16,440
relative to the canonical nucleobases so

107
00:04:20,330 --> 00:04:17,639
I mentioned before that the canonical

108
00:04:21,979 --> 00:04:20,340
nucleobases au G and C do not react with

109
00:04:22,790 --> 00:04:21,989
ribose to form nucleotides or

110
00:04:25,909 --> 00:04:22,800
nucleotides

111
00:04:27,320 --> 00:04:25,919
however tat does and the first

112
00:04:29,240 --> 00:04:27,330
demonstration of this was in our

113
00:04:31,999 --> 00:04:29,250

about five years ago where when you

114
00:04:33,920 --> 00:04:32,009
react app with ribose you get a variety

115
00:04:36,710 --> 00:04:33,930
of nucleoside products the most

116
00:04:38,390 --> 00:04:36,720
predominant of which is the beta c rival

117
00:04:40,550 --> 00:04:38,400
fear anna site the reason that's

118
00:04:42,230 --> 00:04:40,560
important is because we could have ended

119
00:04:44,059 --> 00:04:42,240
up with many different forms of ribose

120
00:04:45,409 --> 00:04:44,069
but the one that popped out in the

121
00:04:48,189 --> 00:04:45,419
greatest abundance was the form of

122
00:04:50,059 --> 00:04:48,199
ribose that is present in RNA today

123
00:04:51,980 --> 00:04:50,069
additionally when incubated with

124
00:04:53,809 --> 00:04:51,990
cyanuric acid in the appropriate buffer

125
00:04:55,610 --> 00:04:53,819
you can get these super molecular

126
00:04:58,189 --> 00:04:55,620
assemblies which you can actually detect

127
00:05:00,980 --> 00:04:58,199
by atomic force microscopy and they have

128
00:05:04,999 --> 00:05:00,990
the appropriate size for this hex ad

129
00:05:06,740 --> 00:05:05,009
structure so it's great that it works

130
00:05:09,589 --> 00:05:06,750
with one nucleobase but we need at least

131
00:05:12,080 --> 00:05:09,599
two to support an information system so

132
00:05:15,529 --> 00:05:12,090
we turned to a different set of

133
00:05:17,959 --> 00:05:15,539
heterocycles this is melamine and this

134
00:05:20,029 --> 00:05:17,969
is barbaric acid we thought these were

135
00:05:22,490 --> 00:05:20,039
attractive because they are structurally

136
00:05:26,089 --> 00:05:22,500
analogous to the extant may you base

137
00:05:27,770 --> 00:05:26,099
pair which again cannot form under

138
00:05:30,499 --> 00:05:27,780

periodically plausible conditions but

139
00:05:33,230 --> 00:05:30,509
perhaps this one can and indeed it does

140
00:05:35,029 --> 00:05:33,240
if you take barbiturate acid or melamine

141
00:05:38,180 --> 00:05:35,039
and react them with ribose 5-phosphate

142
00:05:41,480 --> 00:05:38,190
in water in both cases you get nuclei or

143
00:05:43,640 --> 00:05:41,490
nucleotides and if you take these crude

144
00:05:45,620 --> 00:05:43,650
reaction mixtures that have formed non

145
00:05:47,510 --> 00:05:45,630
canonical nucleotides and combine them

146
00:05:49,999 --> 00:05:47,520
at the appropriate pH you again get this

147
00:05:53,540 --> 00:05:50,009
super molecular assembly appended with

148
00:05:55,159 --> 00:05:53,550
ribose phosphate units and again you can

149
00:05:56,659 --> 00:05:55,169
detect the presence of this super

150
00:05:59,149 --> 00:05:56,669
molecular assembly by atomic force

151
00:06:01,730 --> 00:05:59,159
microscopy another really cool property

152
00:06:05,360 --> 00:06:01,740
of the system is that on the macroscopic

153
00:06:07,459 --> 00:06:05,370
scale these assemblies efficiently

154
00:06:09,080 --> 00:06:07,469
prevent the bulk flow of water so that

155
00:06:11,029 --> 00:06:09,090
you get this hydrogel with a very high

156
00:06:12,649 --> 00:06:11,039
viscosity high enough that it will

157
00:06:17,360 --> 00:06:12,659
support an air bubble without allowing

158
00:06:19,249 --> 00:06:17,370
it to move okay so that was all the work

159
00:06:20,890 --> 00:06:19,259
that was done on trying to elucidate

160
00:06:24,110 --> 00:06:20,900
what could have been the first

161
00:06:25,610 --> 00:06:24,120
recognition unit but that leaves the

162
00:06:27,080 --> 00:06:25,620
question still of what could have been

163
00:06:28,399 --> 00:06:27,090

the first tri functional connector

164
00:06:32,330 --> 00:06:28,409
because I already told you

165
00:06:34,309 --> 00:06:32,340
ribose is only one component among many

166
00:06:37,100 --> 00:06:34,319
that are produced in the model prebiotic

167
00:06:38,329 --> 00:06:37,110
reaction that's typically cited for the

168
00:06:40,670 --> 00:06:38,339
formation of sugars which is the

169
00:06:43,340 --> 00:06:40,680
foremost reaction so

170
00:06:45,290 --> 00:06:43,350
it's not immediately obvious how a

171
00:06:47,300 --> 00:06:45,300
reactive nucleobase could have just

172
00:06:48,890 --> 00:06:47,310
selected ribose over any others because

173
00:06:50,480 --> 00:06:48,900
from a chemists standpoint they

174
00:06:52,310 --> 00:06:50,490
basically all have the same type of

175
00:06:55,879 --> 00:06:52,320
reactivity of via an aldehyde or a

176
00:06:57,770 --> 00:06:55,889
ketone so we decided to test a set of

177
00:06:59,749 --> 00:06:57,780
other sugars to see what the reactivity

178
00:07:01,700 --> 00:06:59,759
with non-canonical nucleobase would be

179
00:07:04,189 --> 00:07:01,710
this is the set we chose we have

180
00:07:07,490 --> 00:07:04,199
pentoses Tetris as hexoses with

181
00:07:09,439 --> 00:07:07,500
different chemical properties and the

182
00:07:11,570 --> 00:07:09,449
essential the basic reaction that we did

183
00:07:13,640 --> 00:07:11,580
was to take the sugar reacted with try

184
00:07:15,500 --> 00:07:13,650
amino / medine either at neutral or

185
00:07:18,350 --> 00:07:15,510
acidic conditions and you can get a

186
00:07:22,510 --> 00:07:18,360
variety of products and we would monitor

187
00:07:24,830 --> 00:07:22,520
all this by NMR so here's the breakdown

188
00:07:26,540 --> 00:07:24,840

now there's a lot of chemical structures

189
00:07:28,580 --> 00:07:26,550
here but what I really want you to take

190
00:07:31,300 --> 00:07:28,590
away from this is that you'll see here

191
00:07:35,000 --> 00:07:31,310
the yields every single sugar worked

192
00:07:36,710 --> 00:07:35,010
every single one that's not really that

193
00:07:39,170 --> 00:07:36,720
surprising from the point of view of

194
00:07:40,969 --> 00:07:39,180
organic chemistry but it is kind of

195
00:07:43,189 --> 00:07:40,979
surprising in our field because it's

196
00:07:45,080 --> 00:07:43,199
often taken for granted that ribose was

197
00:07:47,270 --> 00:07:45,090
first but if you can produce a variety

198
00:07:50,719 --> 00:07:47,280
of sugars along with ribose and they're

199
00:07:53,390 --> 00:07:50,729
all equally but they're all reactive to

200
00:07:54,860 --> 00:07:53,400
an extent with tap then perhaps it's not

201
00:07:57,230 --> 00:07:54,870
a well-founded assumption that you

202
00:08:03,230 --> 00:07:57,240
immediately started with ribose and went

203
00:08:05,570 --> 00:08:03,240
straight to RNA so we wanted to take a

204
00:08:07,430 --> 00:08:05,580
little bit of a closer look at what was

205
00:08:09,050 --> 00:08:07,440
actually forming we did a lot of

206
00:08:12,320 --> 00:08:09,060
different reactions and they're pretty

207
00:08:14,089 --> 00:08:12,330
messy so we took some of the simplest

208
00:08:15,950 --> 00:08:14,099
ones the ones that are based on glucose

209
00:08:18,529 --> 00:08:15,960
and elucidated the structures of the

210
00:08:20,779 --> 00:08:18,539
products so if you have a general Lucas

211
00:08:22,550 --> 00:08:20,789
derivative it can react with tri amino

212
00:08:27,379 --> 00:08:22,560
primitive to form a variety of products

213
00:08:29,899 --> 00:08:27,389

these products either are linked at this

214
00:08:31,490 --> 00:08:29,909
nitrogen atom this nitrogen atom or this

215
00:08:33,380 --> 00:08:31,500
carbon atom those are the most

216
00:08:36,110 --> 00:08:33,390
nucleophilic sites on this molecule tap

217
00:08:37,640 --> 00:08:36,120
and if you assume that the sugar is

218
00:08:40,250 --> 00:08:37,650
always going to be in its six membered

219
00:08:42,440 --> 00:08:40,260
ring form then there's these six

220
00:08:44,300 --> 00:08:42,450
possible products these on the top have

221
00:08:46,550 --> 00:08:44,310
the nuclear base pointing up that's

222
00:08:48,079 --> 00:08:46,560
called beta these on the bottom has a

223
00:08:50,510 --> 00:08:48,089
nuclear base pointing down that's called

224
00:08:53,690 --> 00:08:50,520
alpha and these are the glucose

225
00:08:55,940 --> 00:08:53,700
derivatives that we tested

226
00:08:58,880 --> 00:08:55,950
so when you react tap with glucose you

227
00:09:01,090 --> 00:08:58,890
get all substitutions of tap but you

228
00:09:03,740 --> 00:09:01,100
only get the beta isomers

229
00:09:05,590 --> 00:09:03,750
similarly with glucose 6-phosphate which

230
00:09:08,150 --> 00:09:05,600
is a closer analog to ribose 5-phosphate

231
00:09:11,210 --> 00:09:08,160
and when you try a CN acetyl glucosamine

232
00:09:13,490 --> 00:09:11,220
you also get these beta products but you

233
00:09:16,190 --> 00:09:13,500
do not get the C glycoside you do not

234
00:09:20,480 --> 00:09:16,200
get the glycoside that is connected at

235
00:09:22,910 --> 00:09:20,490
the carbon atom of tap we can talk about

236
00:09:25,400 --> 00:09:22,920
why that might be my favorite hypothesis

237
00:09:27,620 --> 00:09:25,410
is that n acetyl glucosamine is not as

238
00:09:29,480 --> 00:09:27,630

electrophilic and its protonated state

239
00:09:31,550 --> 00:09:29,490
as these so it is not sufficiently

240
00:09:34,850 --> 00:09:31,560
electrophilic to allow for electrophilic

241
00:09:37,070 --> 00:09:34,860
aromatic substitution nevertheless all

242
00:09:38,720 --> 00:09:37,080
of these have formed the beta form so

243
00:09:40,580 --> 00:09:38,730
even from a chemical standpoint there is

244
00:09:41,870 --> 00:09:40,590
a level of selectivity that you get that

245
00:09:45,980 --> 00:09:41,880
could have led to the first nucleic

246
00:09:47,210 --> 00:09:45,990
acids so another thing we wanted to test

247
00:09:49,730 --> 00:09:47,220
what the system was of course the

248
00:09:53,000 --> 00:09:49,740
propensity for it to assemble so i

249
00:09:55,760 --> 00:09:53,010
purified that compound of tap and

250
00:09:57,620 --> 00:09:55,770
glucose 6-phosphate react linked at the

251
00:10:00,430 --> 00:09:57,630
carbon atom and i incubated it with

252
00:10:03,290 --> 00:10:00,440
cyanuric acid at the appropriate pH and

253
00:10:05,150 --> 00:10:03,300
it was strange because it mostly

254
00:10:07,040 --> 00:10:05,160
precipitated and we could see only a

255
00:10:10,220 --> 00:10:07,050
little bit of these tiny assemblies by

256
00:10:12,440 --> 00:10:10,230
atomic force microscopy so we decided

257
00:10:14,450 --> 00:10:12,450
just to not even try and purify it but

258
00:10:16,190 --> 00:10:14,460
start with the crude reaction mixture so

259
00:10:18,800 --> 00:10:16,200
what that means is that I took tap I

260
00:10:20,420 --> 00:10:18,810
reacted it with glucose 6-phosphate I

261
00:10:23,060 --> 00:10:20,430
have that reaction mixture I'm not going

262
00:10:25,780 --> 00:10:23,070
to do anything to it except react or

263
00:10:30,680 --> 00:10:25,790

combine it then with cyanuric acid and

264
00:10:34,580 --> 00:10:30,690
lo and behold we get much more assembly

265
00:10:36,410 --> 00:10:34,590
the assemblies are much longer so first

266
00:10:37,820 --> 00:10:36,420
this is really cool because this is

267
00:10:40,540 --> 00:10:37,830
actually the more prebiotic lee

268
00:10:42,710 --> 00:10:40,550
realistic scenario this one required

269
00:10:45,890 --> 00:10:42,720
purification enervate intervention by a

270
00:10:48,140 --> 00:10:45,900
chemist this one did not so this system

271
00:10:49,910 --> 00:10:48,150
which is more prebiotic irrelevant is

272
00:10:52,520 --> 00:10:49,920
actually the one that supports the super

273
00:10:54,740 --> 00:10:52,530
molecular assembly it's also interesting

274
00:10:56,750 --> 00:10:54,750
because we don't know exactly why this

275
00:10:58,760 --> 00:10:56,760
one supports this assembly better but it

276
00:11:00,740 --> 00:10:58,770
could be because other derivatives of

277
00:11:02,720 --> 00:11:00,750
tap or under rivet eyes tap are also

278
00:11:06,550 --> 00:11:02,730
entering into this assembly and allowing

279
00:11:10,180 --> 00:11:08,860
so during this study we had kind of an

280
00:11:14,050 --> 00:11:10,190
interesting result

281
00:11:15,880 --> 00:11:14,060
we took rib ulos which is a ketose not

282
00:11:18,490 --> 00:11:15,890
an aldose what that means is that its

283
00:11:20,530 --> 00:11:18,500
carbonyl group is flanked by two carbon

284
00:11:23,440 --> 00:11:20,540
atoms rather than just one carbon atom

285
00:11:26,560 --> 00:11:23,450
and then hydrogen so we expected these

286
00:11:28,300 --> 00:11:26,570
products right however that's not at all

287
00:11:30,190 --> 00:11:28,310
what you get well they could be present

288
00:11:32,440 --> 00:11:30,200

but we didn't detect them what we did

289
00:11:35,440 --> 00:11:32,450
detect however were these what are

290
00:11:36,910 --> 00:11:35,450
called al decides they're products that

291
00:11:39,850 --> 00:11:36,920
could have only occurred from the

292
00:11:41,880 --> 00:11:39,860
isomerization of rib ulos that's really

293
00:11:45,640 --> 00:11:41,890
interesting because some of these are

294
00:11:48,720 --> 00:11:45,650
nucleotides they're Ryba signs that's

295
00:11:50,829 --> 00:11:48,730
important because as I said before

296
00:11:53,110 --> 00:11:50,839
ribose it's very difficult to get

297
00:11:55,720 --> 00:11:53,120
exclusively to ribose in a prebiotic the

298
00:11:57,670 --> 00:11:55,730
plausible manner however what if we

299
00:11:59,680 --> 00:11:57,680
could get to rib ulos which then has the

300
00:12:02,590 --> 00:11:59,690
ability to isomerize into ribose or

301
00:12:04,870 --> 00:12:02,600
arabinose turns out that there is a

302
00:12:07,600 --> 00:12:04,880
prebiotic lea plausible route to rib you

303
00:12:09,070 --> 00:12:07,610
loose that does not produce a huge

304
00:12:11,650 --> 00:12:09,080
number of side products like the

305
00:12:13,420 --> 00:12:11,660
foremost reaction it's this reaction of

306
00:12:16,480 --> 00:12:13,430
glyceraldehyde with dihydroxy fumaric

307
00:12:19,530 --> 00:12:16,490
acid this is part of a so-called glyoxal

308
00:12:22,630 --> 00:12:19,540
o scenario which is a hypothesis that is

309
00:12:27,940 --> 00:12:22,640
meant to replace or enhance the for most

310
00:12:30,760 --> 00:12:27,950
reaction so in summary if you take this

311
00:12:32,800 --> 00:12:30,770
hypothesis that RNA is the product of

312
00:12:34,450 --> 00:12:32,810
evolution you can get some really

313
00:12:36,340 --> 00:12:34,460

fruitful results at first it seems

314
00:12:38,230 --> 00:12:36,350
really daunting because there's no

315
00:12:40,810 --> 00:12:38,240
evidence left of what this could have

316
00:12:42,340 --> 00:12:40,820
been so it's a huge chemical space to

317
00:12:44,770 --> 00:12:42,350
explore but if you impose certain

318
00:12:47,530 --> 00:12:44,780
constraints you can really get some

319
00:12:49,030 --> 00:12:47,540
amazing results such as that adenine and

320
00:12:51,070 --> 00:12:49,040
uracil for example were preceded by

321
00:12:52,150 --> 00:12:51,080
bases that were not only more reactive

322
00:12:55,210 --> 00:12:52,160
but had a greater propensity for

323
00:12:58,060 --> 00:12:55,220
self-assembly and this one remained the

324
00:13:01,390 --> 00:12:58,070
details of this still need to be teased

325
00:13:03,460 --> 00:13:01,400
out but we now know that it's not a

326
00:13:04,930 --> 00:13:03,470
great assumption to just go straight to

327
00:13:06,699 --> 00:13:04,940
ribose we have to investigate other

328
00:13:07,870 --> 00:13:06,709
possible tri functional connectors that

329
00:13:10,150 --> 00:13:07,880
could have been present in the first

330
00:13:11,680 --> 00:13:10,160
protein nucleic acids so the thing that

331
00:13:13,690 --> 00:13:11,690
I didn't talk about today was the

332
00:13:16,540 --> 00:13:13,700
ionized linker just to give you a little

333
00:13:19,240 --> 00:13:16,550
snapshot of what we're thinking the

334
00:13:21,280 --> 00:13:19,250
phosphodiester is a dehydrated linkage

335
00:13:24,040 --> 00:13:21,290
perhaps it was preceded by other

336
00:13:27,730 --> 00:13:24,050
dehydrated linkages such as the ester or

337
00:13:29,499 --> 00:13:27,740
the acetal which were more easily formed

338
00:13:32,650 --> 00:13:29,509

on the early Earth than the ester other

339
00:13:33,970 --> 00:13:32,660
than the fossil ester so with that I'd

340
00:13:35,949 --> 00:13:33,980
really like to thank everybody who made

341
00:13:38,730 --> 00:13:35,959
this possible Brian Cafferty was my

342
00:13:42,400 --> 00:13:38,740
mentor and did a lot of the work with

343
00:13:44,129 --> 00:13:42,410
tap ribose Ives Kim Clarke was a postdoc

344
00:13:46,929 --> 00:13:44,139
who did all the atomic force microscopy

345
00:13:49,929 --> 00:13:46,939
for the tap studies

346
00:13:52,059 --> 00:13:49,939
Tyler is our new graduate student who

347
00:13:54,759 --> 00:13:52,069
please go see his poster on the

348
00:13:57,160 --> 00:13:54,769
isomerisation of ribulose and its

349
00:13:59,679 --> 00:13:57,170
reaction with tap Catherine and Megan

350
00:14:02,860 --> 00:13:59,689
were both excellent undergraduates who I

351
00:14:04,360 --> 00:14:02,870
was very privileged to mentor Gary

352
00:14:05,769 --> 00:14:04,370
Shuster and ROM krishnamurthi are our

353
00:14:07,689 --> 00:14:05,779
collaborators who are both excellent

354
00:14:10,540 --> 00:14:07,699
organic chemists and I really especially

355
00:14:12,910 --> 00:14:10,550
like to thank Nicolas Hutt my PI for his

356
00:14:14,259 --> 00:14:12,920
tutelage and his vision and I'd also

357
00:14:16,179 --> 00:14:14,269
like to thank all the members of the

358
00:14:30,519 --> 00:14:16,189
Center for chemical evolution and my lab

359
00:14:34,210 --> 00:14:30,529
and all of you thank you very much David

360
00:14:38,470 --> 00:14:34,220
have you thought about adding some sort

361
00:14:41,860 --> 00:14:38,480
of short gap C peptides or oligopeptides

362
00:14:45,780 --> 00:14:41,870
into your reaction mixtures so maybe you

363
00:14:49,990 --> 00:14:45,790

can get some sort of catalysis and

364
00:14:53,439 --> 00:14:50,000
improve your reactions yeah I could I

365
00:14:56,290 --> 00:14:53,449
can see a way how that would help

366
00:14:58,210 --> 00:14:56,300
we have not tried that but I see like

367
00:14:59,769 --> 00:14:58,220
for example if you formed an ester acid

368
00:15:01,540 --> 00:14:59,779
tile with the an America's ition of the