AbGradCon 2018

1
00:00:00,260 --> 00:00:10,410
[Music]

2
00:00:17,050 --> 00:00:13,930
I'm David I'm a prebiotic chemist

3
00:00:20,230 --> 00:00:17,060
really more of an organic chemist and in

4
00:00:22,090 --> 00:00:20,240
Becky's introduction talk she reviewed

5
00:00:24,370 --> 00:00:22,100
chemical structures to you so I hope you

6
00:00:25,570 --> 00:00:24,380
uh I hope you got that because it's

7
00:00:29,050 --> 00:00:25,580
otherwise it's gonna be a little rough

8
00:00:31,660 --> 00:00:29,060
ride but here we go alright so

9
00:00:33,610 --> 00:00:31,670
fundamentally life is a chemical

10
00:00:35,229 --> 00:00:33,620
phenomenon I don't mean to be

11
00:00:38,680 --> 00:00:35,239
patronizing with this I just want to

12
00:00:40,810 --> 00:00:38,690
highlight that you know you can see a

13
00:00:42,489 --> 00:00:40,820

schematic of DNA but it really does have

14
00:00:43,869 --> 00:00:42,499
fine chemical structure and that fine

15
00:00:48,009 --> 00:00:43,879
chemical structure is important for

16
00:00:49,509 --> 00:00:48,019
elucidating the origin of life so you

17
00:00:52,469 --> 00:00:49,519
know in experiments like the miller-urey

18
00:00:55,439 --> 00:00:52,479
experiment which we're all familiar with

19
00:00:59,169 --> 00:00:55,449
typically the thing that you find are

20
00:01:02,379 --> 00:00:59,179
amino acids so for example the you know

21
00:01:03,729 --> 00:01:02,389
the constituents of a protein but if

22
00:01:05,500 --> 00:01:03,739
what we're trying to figure out is how

23
00:01:07,330 --> 00:01:05,510
another class of biomolecules the

24
00:01:08,860 --> 00:01:07,340
nucleic acids came into existence the

25
00:01:12,070 --> 00:01:08,870
monomers of nucleic acids are

26
00:01:15,070 --> 00:01:12,080
comparatively more complex so compare an

27
00:01:16,780 --> 00:01:15,080
isolated amino acid to an isolated

28
00:01:18,520 --> 00:01:16,790
nucleotide and clearly the nucleotide is

29
00:01:22,890 --> 00:01:18,530
larger and more difficult to assemble

30
00:01:26,020 --> 00:01:22,900
the prebiotic we plausible manner so

31
00:01:28,000 --> 00:01:26,030
before I jump right into my chemistry I

32
00:01:29,980 --> 00:01:28,010
wanted to give you a little bit of an

33
00:01:32,470 --> 00:01:29,990
overview of how biology works today

34
00:01:33,760 --> 00:01:32,480
because that's how we are informed of

35
00:01:38,110 --> 00:01:33,770
what molecules to target in our

36
00:01:40,840 --> 00:01:38,120
prebiotic synthesis so DNA another

37
00:01:42,490 --> 00:01:40,850
schematic DNA is the hereditary molecule

38
00:01:48,330 --> 00:01:42,500

of all life with the exception of some

39
00:01:51,790 --> 00:01:48,340
viruses DNA is transcribed by a protein

40
00:01:54,430 --> 00:01:51,800
into an RNA message and then that RNA is

41
00:01:56,560 --> 00:01:54,440
translated by an enzyme called the

42
00:01:59,190 --> 00:01:56,570
ribosome which emphatically is not

43
00:02:02,800 --> 00:01:59,200
protein based it's RNA based and that

44
00:02:05,380 --> 00:02:02,810
gives you proteins but you require

45
00:02:07,899 --> 00:02:05,390
proteins in order for DNA to replicate

46
00:02:09,520 --> 00:02:07,909
itself so because of this we have a

47
00:02:12,220 --> 00:02:09,530
chicken and egg problem right we need

48
00:02:13,750 --> 00:02:12,230
proteins for DNA and we need DNA to code

49
00:02:17,200 --> 00:02:13,760
for protein so how do we get out of that

50
00:02:18,190 --> 00:02:17,210
cycle well there's there's a clue here

51
00:02:19,240 --> 00:02:18,200
in the central dogma of molecular

52
00:02:23,560 --> 00:02:19,250
biology

53
00:02:26,200 --> 00:02:23,570
which is RNA RNA in the central dogma

54
00:02:28,600 --> 00:02:26,210
fills two different roles one of them is

55
00:02:30,490 --> 00:02:28,610
informational in the form of messenger

56
00:02:32,050 --> 00:02:30,500
RNA and the other one is catalytic in

57
00:02:35,740 --> 00:02:32,060
the form of the ribosome which itself is

58
00:02:37,900 --> 00:02:35,750
a ribozyme of an RNA enzyme so since RNA

59
00:02:39,940 --> 00:02:37,910
has the capability to perform both these

60
00:02:42,520 --> 00:02:39,950
functions which today are mostly

61
00:02:44,020 --> 00:02:42,530
partitioned between DNA and protein it's

62
00:02:47,590 --> 00:02:44,030
thought that RNA played a really

63
00:02:51,360 --> 00:02:47,600

critical role at or close to the origin

64
00:02:53,500 --> 00:02:51,370
of life all right so that leads to this

65
00:02:56,620 --> 00:02:53,510
popular idea called the RNA world

66
00:02:58,600 --> 00:02:56,630
hypothesis which is but before I get

67
00:03:00,580 --> 00:02:58,610
into that I want to explain to you

68
00:03:02,890 --> 00:03:00,590
exactly what RNA is and how its distinct

69
00:03:05,440 --> 00:03:02,900
from DNA so here's that schematic again

70
00:03:07,900 --> 00:03:05,450
and here's the fine structure again RNA

71
00:03:10,830 --> 00:03:07,910
is very similar so if you look at DNA

72
00:03:14,770 --> 00:03:10,840
you have this phosphate deoxyribose

73
00:03:17,199 --> 00:03:14,780
backbone with the nucleobases here RNA

74
00:03:20,199 --> 00:03:17,209
is similar but there are just a few

75
00:03:22,990 --> 00:03:20,209
modifications so in DNA we have the

76
00:03:26,199 --> 00:03:23,000
nucleobases I mean and in RNA we have

77
00:03:28,030 --> 00:03:26,209
the perhaps more perhaps simpler

78
00:03:32,770 --> 00:03:28,040
nucleobase uracil which pairs with

79
00:03:35,550 --> 00:03:32,780
adenine DNA has a hydrogen atom here

80
00:03:38,170 --> 00:03:35,560
where RNA has a hydroxyl group now

81
00:03:40,840 --> 00:03:38,180
superficially that might seem to make

82
00:03:43,420 --> 00:03:40,850
RNA more complicated but actually that

83
00:03:45,810 --> 00:03:43,430
hydroxyl group is easier to produce in a

84
00:03:51,009 --> 00:03:45,820
prebiotic ly plausible manner than the

85
00:03:52,810 --> 00:03:51,019
deoxyribose of DNA and that those small

86
00:03:57,190 --> 00:03:52,820
modifications have profound consequences

87
00:03:59,680 --> 00:03:57,200
in what RNA and DNA are able to do so

88
00:04:01,150 --> 00:03:59,690

DNA is optimized for information storage

89
00:04:02,500 --> 00:04:01,160
and transfer RNA can perform that

90
00:04:05,650 --> 00:04:02,510
function too but because of this

91
00:04:07,990 --> 00:04:05,660
hydroxyl group there is a change in the

92
00:04:09,819 --> 00:04:08,000
bulk structure of RNA which allows it to

93
00:04:13,569 --> 00:04:09,829
more readily access catalytically active

94
00:04:15,520 --> 00:04:13,579
structures all right so now we're at the

95
00:04:17,469 --> 00:04:15,530
RNA world hypothesis which is the idea

96
00:04:19,330 --> 00:04:17,479
that before the DNA protein based

97
00:04:20,620 --> 00:04:19,340
biochemistry of today we had a

98
00:04:24,760 --> 00:04:20,630
biochemistry that was predominantly

99
00:04:27,700 --> 00:04:24,770
based on RNA I just want to really

100
00:04:29,770 --> 00:04:27,710
quickly note that there that idea as

101
00:04:31,839 --> 00:04:29,780
I've just stated it has been contested

102
00:04:32,530 --> 00:04:31,849
of it lately but let's just stay within

103
00:04:36,580 --> 00:04:32,540
that paradigm

104
00:04:39,510 --> 00:04:36,590
for now and I'm gonna give you a

105
00:04:42,580 --> 00:04:39,520
historical perspective on how it's been

106
00:04:45,790 --> 00:04:42,590
investigated so what we want to get to

107
00:04:47,680 --> 00:04:45,800
is this polymer RNA the traditional

108
00:04:49,840 --> 00:04:47,690
approach has been to start from simple

109
00:04:53,560 --> 00:04:49,850
prebiotic precursors sorry there's a

110
00:04:55,360 --> 00:04:53,570
little bit of feedback historical

111
00:04:57,820 --> 00:04:55,370
approach has been to start from simple

112
00:05:00,940 --> 00:04:57,830
prebiotic precursors and build your way

113
00:05:02,440 --> 00:05:00,950

up to the polymer now if you draw it

114
00:05:04,600 --> 00:05:02,450
like this it looks pretty reasonable

115
00:05:07,240 --> 00:05:04,610
right and this is maybe you've heard of

116
00:05:08,710 --> 00:05:07,250
the term paper chemistry it's it's you

117
00:05:10,870 --> 00:05:08,720
can draw it on paper and it looks really

118
00:05:13,510 --> 00:05:10,880
pretty but it's completely wrought with

119
00:05:16,510 --> 00:05:13,520
issues so for example if we want to get

120
00:05:18,220 --> 00:05:16,520
the sugar ribose exclusively that's a

121
00:05:19,840 --> 00:05:18,230
big problem because the chemical

122
00:05:23,980 --> 00:05:19,850
reaction that's typically invoked in

123
00:05:25,810 --> 00:05:23,990
order to produce sugars in a prebiotic

124
00:05:27,280 --> 00:05:25,820
we plausible manner is totally non

125
00:05:29,560 --> 00:05:27,290
selective and produces a variety of

126
00:05:31,810 --> 00:05:29,570
sugars but even if we could produce

127
00:05:34,060 --> 00:05:31,820
ribose exclusively we have a further

128
00:05:37,090 --> 00:05:34,070
problem in that the canonical

129
00:05:38,500 --> 00:05:37,100
nucleobases AUG and c do not react with

130
00:05:39,910 --> 00:05:38,510
ribose in water in the absence of

131
00:05:42,280 --> 00:05:39,920
enzymes the form nucleosides

132
00:05:43,450 --> 00:05:42,290
even if we could form nucleosides though

133
00:05:45,550 --> 00:05:43,460
there are difficulties in

134
00:05:47,830 --> 00:05:45,560
phosphorylation and i'm sure some of you

135
00:05:49,120 --> 00:05:47,840
are aware of attempts to overcome these

136
00:05:51,220 --> 00:05:49,130
difficulties which indeed do

137
00:05:53,100 --> 00:05:51,230
phosphorylate organic compounds but

138
00:05:55,780 --> 00:05:53,110

there remains the problem of

139
00:06:00,370 --> 00:05:55,790
polymerizing those organophosphates to

140
00:06:01,810 --> 00:06:00,380
get this phosphodiester polymer so we in

141
00:06:03,340 --> 00:06:01,820
the HUD lab and in the Center for

142
00:06:06,610 --> 00:06:03,350
chemical evolution in general have this

143
00:06:07,900 --> 00:06:06,620
new approach which is basically the

144
00:06:09,610 --> 00:06:07,910
structures that are present in life

145
00:06:11,440 --> 00:06:09,620
today are not necessarily those that

146
00:06:13,720 --> 00:06:11,450
were present at the very origin of life

147
00:06:15,460 --> 00:06:13,730
and that applies to RNA as well so if

148
00:06:19,780 --> 00:06:15,470
you're willing to accept the idea that

149
00:06:21,670 --> 00:06:19,790
DNA is the descendant of RNA perhaps RNA

150
00:06:24,040 --> 00:06:21,680
is the evolutionary descendant of a

151
00:06:26,650 --> 00:06:24,050
series of pre rnas going all the way

152
00:06:31,939 --> 00:06:26,660
back to this proto-aryan a it's an older

153
00:06:36,290 --> 00:06:33,529
so what we do is we take the nucleic

154
00:06:39,740 --> 00:06:36,300
acids of today and we partition them

155
00:06:41,060 --> 00:06:39,750
into three structural components so one

156
00:06:44,870 --> 00:06:41,070
of them is the ionized linker which

157
00:06:46,430 --> 00:06:44,880
today is phosphate one of them is the

158
00:06:49,670 --> 00:06:46,440
tri functional connector which today is

159
00:06:52,310 --> 00:06:49,680
either ribose in RNA or deoxyribose in

160
00:06:53,570 --> 00:06:52,320
DNA and then we have the recognition

161
00:06:56,540 --> 00:06:53,580
units which are the canonical

162
00:06:57,920 --> 00:06:56,550
nucleobases AUG NC and these structural

163
00:06:59,480 --> 00:06:57,930

components we think would still be

164
00:07:01,040 --> 00:06:59,490
present in the most ancient nucleic

165
00:07:04,150 --> 00:07:01,050
acids but they might have been replaced

166
00:07:06,740 --> 00:07:04,160
with different chemical moieties which

167
00:07:08,390 --> 00:07:06,750
had chemical properties more amenable to

168
00:07:12,740 --> 00:07:08,400
spontaneous formation than this

169
00:07:14,300 --> 00:07:12,750
phosphodiester polymer okay so first I'm

170
00:07:16,730 --> 00:07:14,310
gonna focus on the recognition units of

171
00:07:19,129 --> 00:07:16,740
RNA and how we can start to speculate on

172
00:07:21,740 --> 00:07:19,139
what if what may have preceded the

173
00:07:25,210 --> 00:07:21,750
excellent nucleobases so if you have a

174
00:07:28,100 --> 00:07:25,220
prebiotic ly reasonable milieu of

175
00:07:29,930 --> 00:07:28,110
nucleobases some of them will be the

176
00:07:32,300 --> 00:07:29,940
ones that are present in life today but

177
00:07:33,980 --> 00:07:32,310
surely just out of the natural

178
00:07:34,790 --> 00:07:33,990
trajectory of prebiotic chemistry you're

179
00:07:37,279 --> 00:07:34,800
going to have a bunch of other

180
00:07:37,939 --> 00:07:37,289
heterocycles that are not featured in

181
00:07:40,430 --> 00:07:37,949
life today

182
00:07:42,770 --> 00:07:40,440
so how do we sort out from that complex

183
00:07:45,500 --> 00:07:42,780
mixture a set of nucleobases that can

184
00:07:47,300 --> 00:07:45,510
form an informational system well let's

185
00:07:48,379 --> 00:07:47,310
use the concept of super molecular

186
00:07:50,600 --> 00:07:48,389
assembly to our advantage

187
00:07:52,370 --> 00:07:50,610
some of these heterocycles with will

188
00:07:54,680 --> 00:07:52,380

have the ability to spontaneously self

189
00:07:56,750 --> 00:07:54,690
sort into a super molecular aggregate

190
00:07:59,180 --> 00:07:56,760
and they'll exclude all the other

191
00:08:00,890 --> 00:07:59,190
nucleobases once we had that non

192
00:08:03,499 --> 00:08:00,900
covalent super molecular assembly

193
00:08:07,460 --> 00:08:03,509
perhaps we can use that as a scaffold to

194
00:08:08,899 --> 00:08:07,470
create a covalent polymer so these are

195
00:08:10,879 --> 00:08:08,909
the heterocycles that were most

196
00:08:13,580 --> 00:08:10,889
concerned with they have the ability to

197
00:08:16,339 --> 00:08:13,590
form these super molecular structures by

198
00:08:17,990 --> 00:08:16,349
having two hydrogen bonding phases so

199
00:08:20,330 --> 00:08:18,000
what that means is that they have these

200
00:08:22,189 --> 00:08:20,340
edges that have very polar sides and

201
00:08:24,469 --> 00:08:22,199
they snap together with their pairing

202
00:08:27,529 --> 00:08:24,479
partners to form these hex-head

203
00:08:29,600 --> 00:08:27,539
structures so the bases that we're

204
00:08:31,189 --> 00:08:29,610
concerned with are barbaric acid try me

205
00:08:32,389 --> 00:08:31,199
know permitting or tap as I'm going to

206
00:08:34,850 --> 00:08:32,399
refer to it in the rest of the talk

207
00:08:36,469 --> 00:08:34,860
cyanuric acid and Melanie they all have

208
00:08:38,839 --> 00:08:36,479
the ability to form this hex ad which

209
00:08:40,819 --> 00:08:38,849
forms spontaneously and water the really

210
00:08:42,769 --> 00:08:40,829
cool thing about this hex ad is that

211
00:08:43,820 --> 00:08:42,779
once it's formed it presents a very

212
00:08:45,890 --> 00:08:43,830
large hydro flow

213
00:08:48,530 --> 00:08:45,900

like surface and water and that is very

214
00:08:50,990 --> 00:08:48,540
unfavorable to present to bulk water so

215
00:08:52,460 --> 00:08:51,000
what it does is stack one on top of the

216
00:08:55,370 --> 00:08:52,470
other in order to hide those hydrophobic

217
00:09:00,860 --> 00:08:55,380
faces and you have this super molecular

218
00:09:02,420 --> 00:09:00,870
assembly as a result all right so we

219
00:09:05,120 --> 00:09:02,430
have these non-canonical nuclear bases

220
00:09:07,160 --> 00:09:05,130
that we want to form polymers out of do

221
00:09:08,990 --> 00:09:07,170
they actually react with ribose in order

222
00:09:12,530 --> 00:09:09,000
to form nucleotides turns out that they

223
00:09:14,090 --> 00:09:12,540
do this is work from 2013 from Michael

224
00:09:16,940 --> 00:09:14,100
Chen and Brian Cafferty in the HUD lab

225
00:09:19,340 --> 00:09:16,950
so if you take this hetero cycle tap and

226
00:09:21,620 --> 00:09:19,350
react it with ribose there are a variety

227
00:09:22,940 --> 00:09:21,630
of products that you can form and the

228
00:09:25,430 --> 00:09:22,950
details of this are not important

229
00:09:28,160 --> 00:09:25,440
besides that the one you form in the

230
00:09:30,080 --> 00:09:28,170
greatest yield is the beta rival for

231
00:09:32,600 --> 00:09:30,090
your an aside which what that really

232
00:09:35,180 --> 00:09:32,610
means is it has the same conformation

233
00:09:36,740 --> 00:09:35,190
that nucleus sides in life today have so

234
00:09:38,840 --> 00:09:36,750
the problem is that if you had ribose

235
00:09:40,760 --> 00:09:38,850
there were all these possibilities and

236
00:09:42,320 --> 00:09:40,770
it's not immediately clear why we have

237
00:09:44,360 --> 00:09:42,330
this one in life today

238
00:09:46,130 --> 00:09:44,370

but this suggests that it's just the

239
00:09:49,460 --> 00:09:46,140
natural outcome of the chemical reaction

240
00:09:51,470 --> 00:09:49,470
and if you take this nucleus side which

241
00:09:53,150 --> 00:09:51,480
we call tark and you incubate it with

242
00:09:55,340 --> 00:09:53,160
cyanuric acid in the appropriate buffer

243
00:09:57,380 --> 00:09:55,350
you get these super molecular assemblies

244
00:09:59,510 --> 00:09:57,390
and you can even visualize them by

245
00:10:01,220 --> 00:09:59,520
atomic force microscopy you can see here

246
00:10:03,890 --> 00:10:01,230
that they have the appropriate diameter

247
00:10:07,580 --> 00:10:03,900
for what we predict this super molecular

248
00:10:09,890 --> 00:10:07,590
assembly to be all right so that's cool

249
00:10:11,330 --> 00:10:09,900
but if you want to have an informational

250
00:10:13,970 --> 00:10:11,340
system you need to have at least two

251
00:10:15,560 --> 00:10:13,980
units so just having tap is not enough

252
00:10:17,510 --> 00:10:15,570
so what we're gonna do is take

253
00:10:19,730 --> 00:10:17,520
inspiration again from excellent biology

254
00:10:21,440 --> 00:10:19,740
and make inferences about what extinct

255
00:10:23,990 --> 00:10:21,450
biology could have been like so we have

256
00:10:25,670 --> 00:10:24,000
the au base pair which cannot form

257
00:10:27,950 --> 00:10:25,680
spontaneously in a prebiotic we

258
00:10:30,080 --> 00:10:27,960
plausible men or remember that but

259
00:10:31,670 --> 00:10:30,090
perhaps we can have a similar base pair

260
00:10:33,740 --> 00:10:31,680
which is structurally analogous but that

261
00:10:36,230 --> 00:10:33,750
can form spontaneously improve on acquis

262
00:10:37,490 --> 00:10:36,240
plausible manner just like tark and it

263
00:10:39,710 --> 00:10:37,500

turns out that that is indeed the case

264
00:10:41,270 --> 00:10:39,720
so barbaric acid and melamine both have

265
00:10:43,700 --> 00:10:41,280
the ability to react with ribose in

266
00:10:45,710 --> 00:10:43,710
water ribose 5-phosphate in this case to

267
00:10:48,290 --> 00:10:45,720
form nucleotides and they have the

268
00:10:50,780 --> 00:10:48,300
ability to assemble just like before

269
00:10:52,730 --> 00:10:50,790
at the appropriate pH to form the super

270
00:10:54,590 --> 00:10:52,740
molecular assembly and again you can see

271
00:10:55,940 --> 00:10:54,600
this by atomic force microscopy and

272
00:10:56,840 --> 00:10:55,950
another really cool feature of the

273
00:10:58,850 --> 00:10:56,850
system is that

274
00:11:01,160 --> 00:10:58,860
these fibers are so long and so

275
00:11:03,220 --> 00:11:01,170
interlinked that they prevent the bulk

276
00:11:05,809 --> 00:11:03,230
flow of water so you get this hydrogel

277
00:11:07,790 --> 00:11:05,819
so that's a cool material property but

278
00:11:10,040 --> 00:11:07,800
what's really important here that I want

279
00:11:12,259 --> 00:11:10,050
you to take away is that we have an

280
00:11:13,550 --> 00:11:12,269
information system now as long as we can

281
00:11:16,100 --> 00:11:13,560
figure out a way to polymerize them

282
00:11:18,980 --> 00:11:16,110
because we have two units so really

283
00:11:21,110 --> 00:11:18,990
quickly I want to tell you about another

284
00:11:23,090 --> 00:11:21,120
component of RNA which is the tri

285
00:11:25,519 --> 00:11:23,100
functional connector so just now I was

286
00:11:27,829 --> 00:11:25,529
telling you about how we're not going to

287
00:11:29,569 --> 00:11:27,839
deal with the canonical nucleobases

288
00:11:30,980 --> 00:11:29,579

because they don't react with ribose in

289
00:11:32,840 --> 00:11:30,990
water but if we're willing to accept

290
00:11:34,550 --> 00:11:32,850
that the nucleobases may have been

291
00:11:36,230 --> 00:11:34,560
different we should have that exact same

292
00:11:38,210 --> 00:11:36,240
attitude with all the other components

293
00:11:39,499 --> 00:11:38,220
of RNA so for example we're going to

294
00:11:41,720 --> 00:11:39,509
take the tri functional connector which

295
00:11:44,090 --> 00:11:41,730
today is ribose and see if it could have

296
00:11:45,530 --> 00:11:44,100
been something different now I mentioned

297
00:11:47,780 --> 00:11:45,540
before that it's really difficult to get

298
00:11:49,280 --> 00:11:47,790
ribose in a selective manner because the

299
00:11:51,110 --> 00:11:49,290
reaction that typically is invoked to

300
00:11:52,819 --> 00:11:51,120
produce sugars the foremost reaction is

301
00:11:54,769 --> 00:11:52,829
inherently not selective it produces a

302
00:11:56,210 --> 00:11:54,779
ton of sugar it's like there's a

303
00:11:57,740 --> 00:11:56,220
chromatogram that was shown in Becky's

304
00:11:58,850 --> 00:11:57,750
slides I think that shows the products

305
00:12:00,319 --> 00:11:58,860
of the foremost reaction and you know

306
00:12:02,900 --> 00:12:00,329
there's like a hundred Peaks there's

307
00:12:05,929 --> 00:12:02,910
even more than that so we had this

308
00:12:07,429 --> 00:12:05,939
question if you do naturally produce a

309
00:12:10,100 --> 00:12:07,439
ton of sugars in these prebiotic

310
00:12:12,439 --> 00:12:10,110
reactions can a non-canonical nucleobase

311
00:12:14,329 --> 00:12:12,449
react not just with ribose but perhaps a

312
00:12:16,400 --> 00:12:14,339
suite of them to form

313
00:12:19,579 --> 00:12:16,410

non-canonical nucleosides or glycosides

314
00:12:21,980 --> 00:12:19,589
really now again chemical structure is

315
00:12:23,540 --> 00:12:21,990
terrifying but all I want you to take

316
00:12:25,189 --> 00:12:23,550
away from this is that there's a variety

317
00:12:27,170 --> 00:12:25,199
of sugars which ostensibly have

318
00:12:29,449 --> 00:12:27,180
different chemical properties and may or

319
00:12:31,059 --> 00:12:29,459
may not react with tap so what I'm gonna

320
00:12:36,230 --> 00:12:31,069
do is I'm gonna take a general sugar

321
00:12:37,850 --> 00:12:36,240
just read this word and react it with

322
00:12:41,240 --> 00:12:37,860
tap and you can get a bunch of different

323
00:12:44,660 --> 00:12:41,250
products and it turns out that it works

324
00:12:46,850 --> 00:12:44,670
so in this chart I have the yields here

325
00:12:49,429 --> 00:12:46,860
so we did this either at pH 1 or pH 7

326
00:12:51,350 --> 00:12:49,439
because it turns out that this reaction

327
00:12:53,150 --> 00:12:51,360
happens to be acid catalyzed but I want

328
00:12:54,829 --> 00:12:53,160
you to note that on every single

329
00:12:56,720 --> 00:12:54,839
structure here the reaction worked and

330
00:12:58,329 --> 00:12:56,730
at least one of those conditions every

331
00:13:02,389 --> 00:12:58,339
single one and that's important because

332
00:13:04,670 --> 00:13:02,399
it's often just assumed without any kind

333
00:13:06,410 --> 00:13:04,680
of you know it's assumed a priori that

334
00:13:07,850 --> 00:13:06,420
ribose was first because that's what's

335
00:13:09,769 --> 00:13:07,860
in biology today but that's not

336
00:13:10,079 --> 00:13:09,779
necessarily a good assumption because at

337
00:13:11,910 --> 00:13:10,089
least

338
00:13:14,220 --> 00:13:11,920

from a reactivity standpoint there's

339
00:13:16,079 --> 00:13:14,230
nothing special about ribose all of

340
00:13:17,340 --> 00:13:16,089
these sugars all of them have the

341
00:13:22,259 --> 00:13:17,350
ability to react with the non-canonical

342
00:13:23,400 --> 00:13:22,269
nuclear base okay great so now this is

343
00:13:26,280 --> 00:13:23,410
gonna really be for the chemists in the

344
00:13:28,439 --> 00:13:26,290
room we wanted to take a closer look at

345
00:13:30,720 --> 00:13:28,449
the structural outcome of some of these

346
00:13:32,579 --> 00:13:30,730
reactions now it turns out that glucose

347
00:13:33,569 --> 00:13:32,589
is one of the easiest sugars to study

348
00:13:40,470 --> 00:13:33,579
because it's one of the most well

349
00:13:42,239 --> 00:13:40,480
behaved and structurally congruent so if

350
00:13:43,679 --> 00:13:42,249
we take a glucose derivative and react

351
00:13:46,829 --> 00:13:43,689
it with tap there's basically six

352
00:13:48,660 --> 00:13:46,839
possibilities up here these all have the

353
00:13:50,519 --> 00:13:48,670
tap nucleobase pointing up

354
00:13:52,439 --> 00:13:50,529
that's called beta these all have the

355
00:13:54,389 --> 00:13:52,449
tab nucleobase pointing down that's

356
00:13:56,369 --> 00:13:54,399
called alpha the reason that's important

357
00:13:59,819 --> 00:13:56,379
is because in life today almost all

358
00:14:02,910 --> 00:13:59,829
glycosides of you know of nucleobases

359
00:14:05,040 --> 00:14:02,920
are beta and it turns out the one we get

360
00:14:08,040 --> 00:14:05,050
when we react tap with glucose or

361
00:14:09,809 --> 00:14:08,050
glucose derivative all of the products

362
00:14:11,519 --> 00:14:09,819
are beta so that's very interesting but

363
00:14:14,610 --> 00:14:11,529

that might be intrinsic to glucose

364
00:14:17,069 --> 00:14:14,620
derivatives nevertheless when you get

365
00:14:18,929 --> 00:14:17,079
the reaction of tap with glucose you get

366
00:14:22,019 --> 00:14:18,939
every possible substitution on the tap

367
00:14:24,239 --> 00:14:22,029
molecule because tap turns out to be a

368
00:14:26,449 --> 00:14:24,249
multi dentate nucleophile so you can

369
00:14:28,980 --> 00:14:26,459
have different positions of substitution

370
00:14:30,989 --> 00:14:28,990
glucose 6-phosphate behaves the exact

371
00:14:33,179 --> 00:14:30,999
same way and strangely n acetyl

372
00:14:35,460 --> 00:14:33,189
glucosamine does not tolerate the c

373
00:14:36,840 --> 00:14:35,470
substitution this is a really esoteric

374
00:14:39,569 --> 00:14:36,850
point but that might have to do with

375
00:14:42,290 --> 00:14:39,579
diminished electro felicity of the

376
00:14:45,569 --> 00:14:42,300
relevant intermediate in the reaction

377
00:14:47,809 --> 00:14:45,579
okay so super molecular assembly again

378
00:14:49,980 --> 00:14:47,819
is it possible that these non canonical

379
00:14:51,749 --> 00:14:49,990
nucleus sites which do not feature

380
00:14:52,259 --> 00:14:51,759
ribose have the ability to assemble in

381
00:14:54,509 --> 00:14:52,269
water

382
00:14:56,610 --> 00:14:54,519
well I took one of them and I purified

383
00:14:58,949 --> 00:14:56,620
it just because it's easier to study

384
00:15:00,900 --> 00:14:58,959
that way when you incubate it with

385
00:15:02,280 --> 00:15:00,910
cyanuric acid at the appropriate pH it

386
00:15:04,710 --> 00:15:02,290
forms assemblies but they're really

387
00:15:08,040 --> 00:15:04,720
small this is again an atomic force

388
00:15:10,110 --> 00:15:08,050

microscopy image that's weird but what

389
00:15:11,759 --> 00:15:10,120
if I take the crude reaction mixture so

390
00:15:14,189 --> 00:15:11,769
what that means is I perform a reaction

391
00:15:15,569 --> 00:15:14,199
and I took the reaction without any

392
00:15:18,449 --> 00:15:15,579
purification and mixed it with cyanuric

393
00:15:20,160 --> 00:15:18,459
acid those form very long fibers which

394
00:15:23,069 --> 00:15:20,170
is interesting because this is the more

395
00:15:23,940 --> 00:15:23,079
prebiotic lee reminiscent scenario so

396
00:15:26,160 --> 00:15:23,950
maybe that's telling

397
00:15:28,860 --> 00:15:26,170
something about how these polymers got

398
00:15:30,750 --> 00:15:28,870
going okay really quickly I just wanted

399
00:15:32,070 --> 00:15:30,760
to point out that in this study we had

400
00:15:34,620 --> 00:15:32,080
an interesting result which is that a

401
00:15:36,660 --> 00:15:34,630
sugar called rib ulos we anticipated to

402
00:15:38,880 --> 00:15:36,670
react with tap in this manner to form

403
00:15:40,290 --> 00:15:38,890
these strange nucleus sides but it turns

404
00:15:41,970 --> 00:15:40,300
out that there's no evidence for their

405
00:15:44,550 --> 00:15:41,980
formation rather it forms these

406
00:15:46,680 --> 00:15:44,560
arabinose IDEs and dry besides that's

407
00:15:47,640 --> 00:15:46,690
cool because Ryba sides are nucleus

408
00:15:50,190 --> 00:15:47,650
sites those are the things that are

409
00:15:52,050 --> 00:15:50,200
present in life today now why are we

410
00:15:53,190 --> 00:15:52,060
excited about this I told you earlier

411
00:15:55,050 --> 00:15:53,200
that it's really difficult to get to

412
00:15:56,790 --> 00:15:55,060
ribose in a prebiotic ly possible manner

413
00:15:58,710 --> 00:15:56,800

but it turns out that rib ulos is a

414
00:16:00,540 --> 00:15:58,720
little bit easier there's a synthesis by

415
00:16:03,360 --> 00:16:00,550
ROM Christian Murphy where you can get

416
00:16:05,670 --> 00:16:03,370
to Regulus and in our system we think

417
00:16:08,640 --> 00:16:05,680
what's going on is that it's isomerizing

418
00:16:10,200 --> 00:16:08,650
in situ to ribose and arabinose and then

419
00:16:12,180 --> 00:16:10,210
reacting with tap to form these

420
00:16:14,370 --> 00:16:12,190
nucleotides so that's pretty cool this

421
00:16:16,530 --> 00:16:14,380
is the proposed prebiotic synthesis of

422
00:16:19,470 --> 00:16:16,540
rib EULA's and if you want to learn more

423
00:16:24,570 --> 00:16:19,480
please see Tyler's poster which is all

424
00:16:27,060 --> 00:16:24,580
about this okay so just to recap we are

425
00:16:28,350 --> 00:16:27,070
taking the stance that the structures

426
00:16:29,760 --> 00:16:28,360
that are present in life today are not

427
00:16:31,680 --> 00:16:29,770
necessarily those that were present at

428
00:16:35,100 --> 00:16:31,690
the origin of life and most importantly

429
00:16:36,780 --> 00:16:35,110
RNA was not emphatically first so if we

430
00:16:38,970 --> 00:16:36,790
take this approach we get some really

431
00:16:41,370 --> 00:16:38,980
interesting results the nucleobases

432
00:16:42,420 --> 00:16:41,380
could have been different we go to ones

433
00:16:44,250 --> 00:16:42,430
that are more reactive and have a

434
00:16:45,630 --> 00:16:44,260
greater propensity for self-assembly the

435
00:16:49,430 --> 00:16:45,640
sugars could have been different in that

436
00:16:51,480 --> 00:16:49,440
sorting that out is that's gonna be fine

437
00:16:52,920 --> 00:16:51,490
we didn't I didn't talk about the

438
00:16:55,080 --> 00:16:52,930

ionized linker but we are investigating

439
00:16:59,190 --> 00:16:55,090
that in our lab and if you want to learn

440
00:17:01,530 --> 00:16:59,200
more just ask me later okay

441
00:17:03,360 --> 00:17:01,540
so I just want to thank everyone who

442
00:17:05,400 --> 00:17:03,370
made this possible Brian Cafferty was my

443
00:17:06,510 --> 00:17:05,410
mentor when I first joined the lab Kim

444
00:17:07,980 --> 00:17:06,520
Clark did all the atomic force

445
00:17:09,569 --> 00:17:07,990
microscopy that you just saw

446
00:17:11,610 --> 00:17:09,579
Tyler's our new graduate student who's

447
00:17:13,290 --> 00:17:11,620
taking on all this rib you low stuff I

448
00:17:15,270 --> 00:17:13,300
was really lucky to have really talented

449
00:17:17,850 --> 00:17:15,280
undergraduates Catherine and Megan and

450
00:17:18,600 --> 00:17:17,860
really great mentors especially ipi

451
00:17:27,329 --> 00:17:18,610
nicholas hi

452
00:17:40,660 --> 00:17:29,289
all right we have time for a couple

453
00:17:49,850 --> 00:17:47,540
hi we talk in your walk with interaction

454
00:17:52,220 --> 00:17:49,860
with Daffy and barbecue rig acid do you

455
00:17:55,220 --> 00:17:52,230
think that the interaction between

456
00:17:58,220 --> 00:17:55,230
tavern barbecue rig acid and their

457
00:18:00,680 --> 00:17:58,230
ribose phosphate derivatives is that

458
00:18:02,540 --> 00:18:00,690
depending on their inherent chirality as

459
00:18:03,890 --> 00:18:02,550
well could be

460
00:18:05,630 --> 00:18:03,900
so you're talking about the chirality of

461
00:18:11,990 --> 00:18:05,640
those nucleotides has endowed by the

462
00:18:14,510 --> 00:18:12,000
sugar yeah okay it could but we perform

463
00:18:16,190 --> 00:18:14,520

this study with commercially supplied

464
00:18:18,200 --> 00:18:16,200
sugars so they are in fatica ly not

465
00:18:19,970 --> 00:18:18,210
receiving they're all in an tio cured so

466
00:18:23,300 --> 00:18:19,980
we have not investigated that yet but

467
00:18:30,560 --> 00:18:23,310
there is research in our lab which find

468
00:18:32,360 --> 00:18:30,570
me later I'll tell you about that would

469
00:18:34,430 --> 00:18:32,370
it be possible then or have you tried

470
00:18:37,340 --> 00:18:34,440
something like that in which a chiral

471
00:18:42,560 --> 00:18:37,350
the or one part of it resolves another

472
00:18:43,910 --> 00:18:42,570
which is its that someone else's work in

473
00:18:58,750 --> 00:18:43,920
my lab and I can totally tell you all

474
00:19:04,960 --> 00:19:02,500
my grater in general what glucosides

475
00:19:08,410 --> 00:19:04,970
also something chromatic linked to a

476
00:19:10,360 --> 00:19:08,420
sugar a very very common implants which

477
00:19:12,640 --> 00:19:10,370
are used for all type of signaling and

478
00:19:15,700 --> 00:19:12,650
regulation do you think that if before

479
00:19:18,520 --> 00:19:15,710
was just on RNA and DNA really need us

480
00:19:20,080 --> 00:19:18,530
in understanding for example ancient

481
00:19:22,510 --> 00:19:20,090
signaling pathways or action networks

482
00:19:24,220 --> 00:19:22,520
because this thing's they might look

483
00:19:34,260 --> 00:19:24,230
more similar to work like plants and

484
00:19:36,100 --> 00:19:34,270
bacteria nowadays yeah yeah yeah okay so

485
00:19:38,500 --> 00:19:36,110
related to what you're saying

486
00:19:40,690 --> 00:19:38,510
it's interesting to think about how so

487
00:19:42,850 --> 00:19:40,700
many cofactors in life are basically

488
00:19:46,750 --> 00:19:42,860

nucleotide it's like NADH and stuff like

489
00:19:48,910 --> 00:19:46,760
that I think that that might bear a clue

490
00:19:51,610 --> 00:19:48,920
as to the origin of nucleic acids but it

491
00:19:53,770 --> 00:19:51,620
you know also possibly the origin of a

492
00:19:56,620 --> 00:19:53,780
more rudimentary biological system in

493
00:19:58,960 --> 00:19:56,630
general but we can talk yeah that can go

494
00:19:59,670 --> 00:19:58,970
into many avenues so I'll just leave it

495
00:20:01,870 --> 00:19:59,680
at that

496
00:20:03,940 --> 00:20:01,880
alright so in the interest of time we're