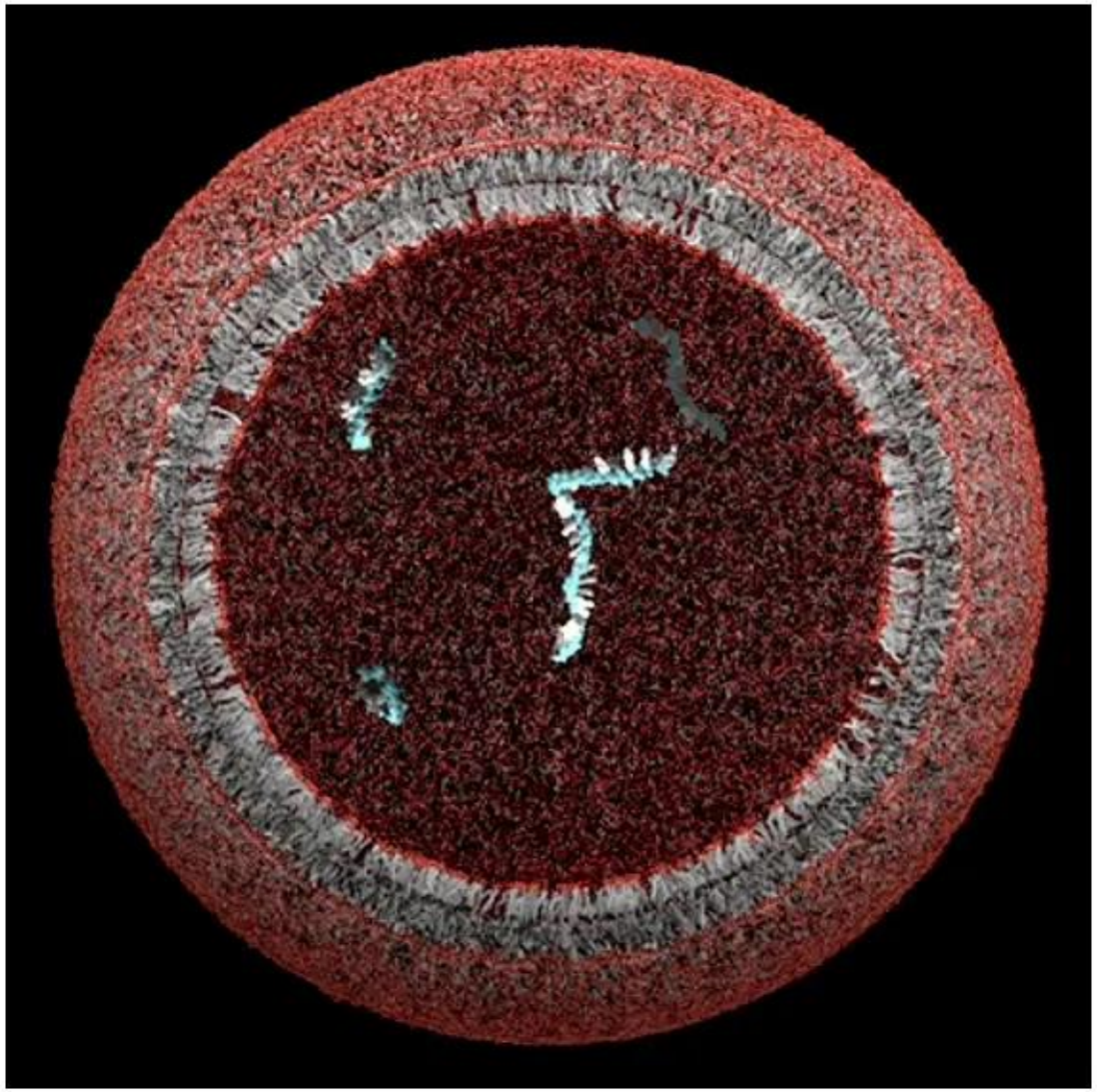
A Primitive Compartment



Szostak Lab

1
00:00:18,550 --> 00:00:16,070
my

2
00:00:20,470 --> 00:00:18,560
the modern cell is a very complex system

3
00:00:22,710 --> 00:00:20,480
consisting of many parts

4
00:00:24,150 --> 00:00:22,720
which perform very specific functions

5
00:00:26,070 --> 00:00:24,160
we've learned a lot about how

6
00:00:27,509 --> 00:00:26,080
the cell works in the last 20 or 30

7
00:00:30,470 --> 00:00:27,519
years but there's still more

8
00:00:32,310 --> 00:00:30,480
questions to be answered one of these

9
00:00:34,229 --> 00:00:32,320
questions is how exactly the

10
00:00:36,709 --> 00:00:34,239
initial cell emerged and evolved in the

11
00:00:38,389 --> 00:00:36,719
first place and one of the hypotheses is

12
00:00:40,549 --> 00:00:38,399
that a primitive compartment

13
00:00:42,549 --> 00:00:40,559

or otherwise known as a protocell was

14
00:00:44,869 --> 00:00:42,559
the first form that eventually evolved

15
00:00:47,110 --> 00:00:44,879
into modern cells

16
00:00:48,950 --> 00:00:47,120
this leads us to origins of life

17
00:00:51,350 --> 00:00:48,960
research where we focus on how

18
00:00:53,990 --> 00:00:51,360
the chemistries available on early earth

19
00:00:56,150 --> 00:00:54,000
also known as prebiotic chemistry

20
00:00:58,229 --> 00:00:56,160
assembled into the first compartments on

21
00:01:01,590 --> 00:00:58,239
earth and how these compartments

22
00:01:03,110 --> 00:01:01,600
evolved into modern cells

23
00:01:04,710 --> 00:01:03,120
compartments in particular are very

24
00:01:06,630 --> 00:01:04,720
crucial to the origins of life

25
00:01:07,990 --> 00:01:06,640
as they perform a number of very

26
00:01:10,870 --> 00:01:08,000
essential functions to

27
00:01:12,390 --> 00:01:10,880
a primitive system such as concentrating

28
00:01:17,190 --> 00:01:12,400
and segregating reactants

29
00:01:20,550 --> 00:01:19,390
one process that allows primitive

30
00:01:23,109 --> 00:01:20,560
compartmentalization

31
00:01:23,830 --> 00:01:23,119
is liquid-liquid phase separation this

32
00:01:25,190 --> 00:01:23,840
process

33
00:01:27,510 --> 00:01:25,200
results in the formation of

34
00:01:29,990 --> 00:01:27,520
membrane-free droplets similar to

35
00:01:31,469 --> 00:01:30,000
colloids or other soft matter and these

36
00:01:33,510 --> 00:01:31,479
droplets can allow

37
00:01:35,590 --> 00:01:33,520
compartmentalization and exchange of

38
00:01:37,670 --> 00:01:35,600

molecules between phases

39
00:01:39,429 --> 00:01:37,680
in fact phase separation is present in

40
00:01:41,830 --> 00:01:39,439
biology where a number of

41
00:01:43,109 --> 00:01:41,840
membraneless organelles exist in our

42
00:01:46,310 --> 00:01:43,119
modern cells such as

43
00:01:48,230 --> 00:01:46,320
stress granules or chromatin

44
00:01:50,310 --> 00:01:48,240
one of the systems that we like to study

45
00:01:52,550 --> 00:01:50,320
as model systems that are

46
00:01:54,389 --> 00:01:52,560
liquid liquid phase separated are called

47
00:01:56,389 --> 00:01:54,399
complex coaster rates

48
00:01:58,149 --> 00:01:56,399
these structures are formed from the

49
00:01:59,510 --> 00:01:58,159
binding of oppositely charged

50
00:02:02,550 --> 00:01:59,520
biopolymers such as

51
00:02:05,109 --> 00:02:02,560
a positively charged peptide and a

52
00:02:05,910 --> 00:02:05,119
negatively charged nucleic acid and the

53
00:02:08,229 --> 00:02:05,920
result is

54
00:02:11,350 --> 00:02:08,239
a membraneless droplet concentrated in

55
00:02:13,750 --> 00:02:11,360
both of these phases

56
00:02:14,390 --> 00:02:13,760
coastal rates actually perform a number

57
00:02:16,869 --> 00:02:14,400
of very

58
00:02:18,550 --> 00:02:16,879
important primitive functions such as

59
00:02:20,790 --> 00:02:18,560
the ability to concentrate

60
00:02:22,869 --> 00:02:20,800
biomolecules such as nucleotides or

61
00:02:24,470 --> 00:02:22,879
nucleic acids

62
00:02:26,630 --> 00:02:24,480
coaster rates have also been shown to

63
00:02:27,910 --> 00:02:26,640

grow and divide through external forces

64
00:02:31,670 --> 00:02:27,920
such as

65
00:02:33,910 --> 00:02:31,680
physical agitation or electric fields

66
00:02:35,350 --> 00:02:33,920
coaster rates can have their structural

67
00:02:37,030 --> 00:02:35,360
complexity increased

68
00:02:39,030 --> 00:02:37,040
through the assembly of multi-phase

69
00:02:41,030 --> 00:02:39,040
compartments each with very specific

70
00:02:43,030 --> 00:02:41,040
chemical affinities

71
00:02:44,229 --> 00:02:43,040
and also coaster rates can scaffold

72
00:02:46,710 --> 00:02:44,239
membrane assembly

73
00:02:47,430 --> 00:02:46,720
suggesting perhaps one transition state

74
00:02:49,589 --> 00:02:47,440
between

75
00:02:52,470 --> 00:02:49,599
a membrane list and a membrane-bound

76
00:02:55,670 --> 00:02:52,480
primitive compartment

77
00:02:58,550 --> 00:02:55,680
in our studies we focused on

78
00:03:00,869 --> 00:02:58,560
another way to potentially increase the

79
00:03:02,710 --> 00:03:00,879
structural complexity of coastal rates

80
00:03:04,630 --> 00:03:02,720
and this is through the incorporation of

81
00:03:11,270 --> 00:03:04,640
dna liquid crystals

82
00:03:13,110 --> 00:03:11,280
short duplex oligomers bind together and

83
00:03:15,270 --> 00:03:13,120
aggregate end to end forming these long

84
00:03:18,149 --> 00:03:15,280
stiff rods these stiff rods

85
00:03:20,390 --> 00:03:18,159
actually will bundle together forming

86
00:03:23,589 --> 00:03:20,400
these nice

87
00:03:26,630 --> 00:03:23,599
patterns that can be observed in

88
00:03:28,869 --> 00:03:26,640

polarization microscopy and we sought to

89
00:03:30,789 --> 00:03:28,879
combine this liquid crystal structure

90
00:03:32,949 --> 00:03:30,799
with a coaster rate structure

91
00:03:36,949 --> 00:03:32,959
through the addition of a cationic

92
00:03:42,869 --> 00:03:39,830
indeed we noticed that through addition

93
00:03:45,670 --> 00:03:42,879
of polylysine to these dna structures

94
00:03:47,430 --> 00:03:45,680
we were able to find the co-localization

95
00:03:49,910 --> 00:03:47,440
of liquid crystal structures

96
00:03:51,350 --> 00:03:49,920
seen below and the membraneless droplet

97
00:03:53,429 --> 00:03:51,360
structure seen above through the

98
00:03:55,750 --> 00:03:53,439
different types of microscopy

99
00:03:57,350 --> 00:03:55,760
this structure is likely caused by the

100
00:04:00,550 --> 00:03:57,360
end-to-end stacking interaction

101
00:04:03,750 --> 00:04:00,560
of these dna duplexes interacting with

102
00:04:06,070 --> 00:04:03,760
the polylysine peptides

103
00:04:07,990 --> 00:04:06,080
so we actually were able to find these

104
00:04:10,949 --> 00:04:08,000
structures but they're actually

105
00:04:12,710 --> 00:04:10,959
only exist under very specific salt

106
00:04:16,469 --> 00:04:12,720
conditions

107
00:04:18,629 --> 00:04:16,479
here we show that the structure of these

108
00:04:21,670 --> 00:04:18,639
liquid crystal coaster rate structures

109
00:04:24,710 --> 00:04:21,680
as we call them is modulated

110
00:04:25,510 --> 00:04:24,720
through the modulation of sodium

111
00:04:28,070 --> 00:04:25,520
chloride

112
00:04:29,430 --> 00:04:28,080
so for example at lower concentrations

113
00:04:31,030 --> 00:04:29,440

of sodium chloride

114
00:04:33,350 --> 00:04:31,040
what we see are precipitate-like

115
00:04:36,270 --> 00:04:33,360
structures at 800 millimolars

116
00:04:37,430 --> 00:04:36,280
we see of sodium chloride we see

117
00:04:38,950 --> 00:04:37,440
co-localization

118
00:04:40,469 --> 00:04:38,960
of the liquid crystal coastal rate

119
00:04:43,350 --> 00:04:40,479
structure and through

120
00:04:45,670 --> 00:04:43,360
increasing sodium chloride we see first

121
00:04:46,629 --> 00:04:45,680
the disassembly of the liquid crystal

122
00:04:48,710 --> 00:04:46,639
structure

123
00:04:50,550 --> 00:04:48,720
followed by the disassembly of the

124
00:04:53,909 --> 00:04:50,560
droplets themselves

125
00:04:55,990 --> 00:04:53,919
we believe that this

126
00:04:57,830 --> 00:04:56,000
property is due to the fact that

127
00:05:00,390 --> 00:04:57,840
increasing salt concentration

128
00:05:01,430 --> 00:05:00,400
will help to shield the interactions

129
00:05:04,310 --> 00:05:01,440
between the

130
00:05:05,909 --> 00:05:04,320
cationic peptide and the anionic dna

131
00:05:07,909 --> 00:05:05,919
backbone suggesting that

132
00:05:10,310 --> 00:05:07,919
higher salt concentrations result in

133
00:05:12,629 --> 00:05:10,320
less interaction between those polymers

134
00:05:14,150 --> 00:05:12,639
and lower salt concentration results in

135
00:05:16,469 --> 00:05:14,160
stronger interaction between those

136
00:05:18,710 --> 00:05:16,479
polymers

137
00:05:21,110 --> 00:05:18,720
we also did an experiment where we

138
00:05:24,870 --> 00:05:21,120

engineered a dna duplex but with

139
00:05:26,790 --> 00:05:24,880
two base overhangs and so this structure

140
00:05:28,950 --> 00:05:26,800
actually resulted in the formation of

141
00:05:30,629 --> 00:05:28,960
coaster vates but no liquid crystal

142
00:05:31,510 --> 00:05:30,639
structures and we believe that this is

143
00:05:35,029 --> 00:05:31,520
because

144
00:05:35,590 --> 00:05:35,039
the 2t base overhang actually inhibits

145
00:05:46,870 --> 00:05:35,600
the

146
00:05:48,629 --> 00:05:46,880
processes on early earth could have also

147
00:05:50,390 --> 00:05:48,639
modulated the structure of these liquid

148
00:05:52,150 --> 00:05:50,400
crystal coaster rates and here we

149
00:05:54,150 --> 00:05:52,160
subjected the liquid crystal coastal

150
00:05:56,390 --> 00:05:54,160
rate structures to dehydration

151
00:05:57,270 --> 00:05:56,400
a process that could have been affected

152
00:06:00,150 --> 00:05:57,280
on earlier

153
00:06:00,950 --> 00:06:00,160
through for example evaporation caused

154
00:06:04,790 --> 00:06:00,960
by

155
00:06:08,070 --> 00:06:04,800
seasonal or day night changes so here

156
00:06:08,469 --> 00:06:08,080
we see from a to e first the existence

157
00:06:10,870 --> 00:06:08,479
of

158
00:06:12,870 --> 00:06:10,880
a precipitate-like structure this

159
00:06:14,790 --> 00:06:12,880
precipitate like structure transitions

160
00:06:16,950 --> 00:06:14,800
into a liquid crystal

161
00:06:18,070 --> 00:06:16,960
coastal rate structure shown in b and c

162
00:06:20,309 --> 00:06:18,080
and slowly

163
00:06:21,749 --> 00:06:20,319

through further dehydration the liquid

164
00:06:23,110 --> 00:06:21,759
crystal coaster rates

165
00:06:24,870 --> 00:06:23,120
of the liquid crystals start to

166
00:06:27,510 --> 00:06:24,880
disassemble resulting in

167
00:06:29,270 --> 00:06:27,520
only coaster based structures in d and

168
00:06:31,350 --> 00:06:29,280
finally in e we see that the

169
00:06:32,629 --> 00:06:31,360
entire coaster rate structure has been

170
00:06:35,990 --> 00:06:32,639
disassembled

171
00:06:42,790 --> 00:06:36,000
here is a video showing the similar

172
00:06:46,390 --> 00:06:45,350
and we believe that this process is due

173
00:06:49,589 --> 00:06:46,400
to the fact that

174
00:06:51,670 --> 00:06:49,599
the dehydration actually results in

175
00:06:53,510 --> 00:06:51,680
up concentration of the sodium chloride

176
00:06:55,670 --> 00:06:53,520
in solution such that

177
00:06:57,110 --> 00:06:55,680
by increasing the sodium chloride in the

178
00:07:02,710 --> 00:06:57,120
solution

179
00:07:06,950 --> 00:07:02,720
again similar to what we saw in the salt

180
00:07:09,110 --> 00:07:06,960
the salt titration experiments

181
00:07:11,749 --> 00:07:09,120
we see that the system transitions from

182
00:07:14,790 --> 00:07:11,759
precipitate to liquid crystal classivate

183
00:07:17,909 --> 00:07:14,800
to non-liquid crystal coastal rate to a

184
00:07:22,870 --> 00:07:20,390
next we wondered whether the system

185
00:07:25,909 --> 00:07:22,880
again could be modulated through

186
00:07:26,550 --> 00:07:25,919
various other primitive processes that

187
00:07:29,110 --> 00:07:26,560
would have been

188
00:07:30,790 --> 00:07:29,120

plausible and so here we study how heat

189
00:07:32,390 --> 00:07:30,800
can affect the structure of the liquid

190
00:07:36,150 --> 00:07:32,400
crystal classivates

191
00:07:38,629 --> 00:07:36,160
so we first started at 20 degrees

192
00:07:39,350 --> 00:07:38,639
upon bringing the system to 50 degrees

193
00:07:42,629 --> 00:07:39,360
we see

194
00:07:44,390 --> 00:07:42,639
very little structural change but

195
00:07:46,629 --> 00:07:44,400
upon bringing the system up to 60

196
00:07:48,950 --> 00:07:46,639
degrees we see a transition from the

197
00:07:51,189 --> 00:07:48,960
precipitate-like structures to a

198
00:07:54,710 --> 00:07:51,199
co-localized liquid crystal class survey

199
00:07:56,710 --> 00:07:54,720
like structure seen here and upon

200
00:07:58,150 --> 00:07:56,720
further increasing the temperature to 70

201
00:07:58,950 --> 00:07:58,160
degrees we see the liquid crystal

202
00:08:01,749 --> 00:07:58,960
structures

203
00:08:03,430 --> 00:08:01,759
disassembly disassembling resulting in

204
00:08:07,830 --> 00:08:03,440
only the

205
00:08:10,710 --> 00:08:07,840
non-liquid crystal coaster rate droplets

206
00:08:11,990 --> 00:08:10,720
we next decrease the temperature and so

207
00:08:15,430 --> 00:08:12,000
here we decreased the temperature

208
00:08:17,350 --> 00:08:15,440
to 50 degrees and no significant changes

209
00:08:19,589 --> 00:08:17,360
were seen

210
00:08:21,749 --> 00:08:19,599
upon decrease to 40 degrees we noticed

211
00:08:24,830 --> 00:08:21,759
that the liquid crystal classroots

212
00:08:26,390 --> 00:08:24,840
started to reappear and they were

213
00:08:28,710 --> 00:08:26,400

co-exist

214
00:08:30,869 --> 00:08:28,720
with the non-liquid crystal coaster

215
00:08:32,870 --> 00:08:30,879
rates seen here and so here in blue

216
00:08:34,709 --> 00:08:32,880
it's one type of liquid crystal the

217
00:08:36,389 --> 00:08:34,719
pneumatic phase and in red it's another

218
00:08:40,230 --> 00:08:36,399
type of liquid crystal the

219
00:08:42,550 --> 00:08:40,240
columnar phase upon further decreases in

220
00:08:44,149 --> 00:08:42,560
temperature we see more and more

221
00:08:46,470 --> 00:08:44,159
appearance of these liquid crystal

222
00:08:48,389 --> 00:08:46,480
coaster rate structures

223
00:08:50,630 --> 00:08:48,399
and finally decreasing the structure

224
00:08:52,870 --> 00:08:50,640
down to 10 degrees

225
00:08:54,389 --> 00:08:52,880
we actually see a majority of these

226
00:08:57,590 --> 00:08:54,399
structures being liquid crystal

227
00:09:01,430 --> 00:08:59,110
what's most interesting about this

228
00:09:04,070 --> 00:09:01,440
system is in fact that

229
00:09:04,470 --> 00:09:04,080
at very low temperatures before and

230
00:09:06,150 --> 00:09:04,480
after

231
00:09:08,150 --> 00:09:06,160
heating and cooling cycle the structure

232
00:09:10,710 --> 00:09:08,160
is very different for example

233
00:09:11,269 --> 00:09:10,720
at 20 degrees before heating and cooling

234
00:09:13,750 --> 00:09:11,279
we see

235
00:09:14,630 --> 00:09:13,760
predominantly the precipitate form

236
00:09:16,870 --> 00:09:14,640
whereas

237
00:09:18,790 --> 00:09:16,880
at 10 degrees after heating and cooling

238
00:09:20,310 --> 00:09:18,800

we see predominantly a liquid crystal

239
00:09:22,150 --> 00:09:20,320
coaster rate form

240
00:09:24,949 --> 00:09:22,160
and we believe that this is due to the

241
00:09:26,790 --> 00:09:24,959
fact that it's very likely that the

242
00:09:28,389 --> 00:09:26,800
liquid crystal class survey form is the

243
00:09:30,070 --> 00:09:28,399
most stable form and so

244
00:09:31,670 --> 00:09:30,080
the system requires a heating and

245
00:09:33,590 --> 00:09:31,680
cooling cycle or

246
00:09:34,790 --> 00:09:33,600
some other people also refer to this as

247
00:09:38,230 --> 00:09:34,800
an annealing cycle

248
00:09:40,150 --> 00:09:38,240
to find this most stable form

249
00:09:41,509 --> 00:09:40,160
so here's a summary figure showing what

250
00:09:43,670 --> 00:09:41,519
we believe is happening

251
00:09:45,190 --> 00:09:43,680
molecularly within these liquid crystal

252
00:09:48,230 --> 00:09:45,200
coaster rates

253
00:09:52,389 --> 00:09:48,240
upon increasing heat and salinity we see

254
00:09:55,190 --> 00:09:52,399
a transition in the phases first in red

255
00:09:57,030 --> 00:09:55,200
the existence of the columnar liquid

256
00:09:58,070 --> 00:09:57,040
crystal phase with the coaster rate

257
00:10:01,110 --> 00:09:58,080
phase where

258
00:10:04,630 --> 00:10:01,120
perhaps the dna rods in blue

259
00:10:06,630 --> 00:10:04,640
are interacting with the peptide strands

260
00:10:08,710 --> 00:10:06,640
in red and the rods have bundled

261
00:10:11,509 --> 00:10:08,720
together into hexagonal like

262
00:10:13,670 --> 00:10:11,519
forms increasing the heat and salinity

263
00:10:14,150 --> 00:10:13,680

results in the slight disassembly of

264
00:10:16,710 --> 00:10:14,160
these

265
00:10:18,310 --> 00:10:16,720
hexagonal bundles but still the

266
00:10:20,150 --> 00:10:18,320
existence of the rods

267
00:10:21,750 --> 00:10:20,160
and the interaction with the peptides

268
00:10:23,910 --> 00:10:21,760
suggesting the

269
00:10:25,190 --> 00:10:23,920
co-localization between here the

270
00:10:28,310 --> 00:10:25,200
cholesteric phase

271
00:10:30,550 --> 00:10:28,320
and the liquid crystal phase next upon

272
00:10:34,069 --> 00:10:30,560
further increases in heat insulinity

273
00:10:37,590 --> 00:10:34,079
we see the disassembly of these

274
00:10:40,230 --> 00:10:37,600
long rods resulting in shorter dna

275
00:10:42,310 --> 00:10:40,240
duplexes interacting with the peptides

276
00:10:43,430 --> 00:10:42,320
which results in formation of non-liquid

277
00:10:47,110 --> 00:10:43,440
crystal

278
00:10:50,069 --> 00:10:47,120
coaster rate droplets and finally upon

279
00:10:51,190 --> 00:10:50,079
high heats or high salinities the entire

280
00:10:53,670 --> 00:10:51,200
assembly

281
00:10:55,269 --> 00:10:53,680
disassembles so the dna no longer

282
00:10:57,430 --> 00:10:55,279
interacts with the peptides

283
00:11:00,310 --> 00:10:57,440
resulting in disassembly of the entire

284
00:11:02,310 --> 00:11:00,320
droplet phase

285
00:11:03,910 --> 00:11:02,320
so for those who are interested in

286
00:11:05,030 --> 00:11:03,920
learning more details about these

287
00:11:07,110 --> 00:11:05,040
studies

288
00:11:09,670 --> 00:11:07,120

here's information about two papers that

289
00:11:11,910 --> 00:11:09,680
were published last year

290
00:11:14,069 --> 00:11:11,920
they have a lot more details of the

291
00:11:14,949 --> 00:11:14,079
experiments that we performed and some

292
00:11:17,509 --> 00:11:14,959
of the theory

293
00:11:18,710 --> 00:11:17,519
that goes into these studies so i

294
00:11:21,670 --> 00:11:18,720
encourage you to

295
00:11:22,150 --> 00:11:21,680
look up these papers if you have more

296
00:11:25,190 --> 00:11:22,160
interest

297
00:11:27,829 --> 00:11:25,200
in learning some of the details

298
00:11:29,670 --> 00:11:27,839
so finally i'd like to thank all of the

299
00:11:31,509 --> 00:11:29,680
funding sources that helped to make this

300
00:11:33,670 --> 00:11:31,519
research possible including those from

301
00:11:38,470 --> 00:11:33,680
tokyo institute of technology

302
00:11:38,790 --> 00:11:38,480
jsps kakenhei japan astrobiology center

303
00:11:41,030 --> 00:11:38,800
and

304
00:11:42,230 --> 00:11:41,040
in particular this project was a

305
00:11:44,710 --> 00:11:42,240
collaboration

306
00:11:46,949 --> 00:11:44,720
through the french embassy in japan

307
00:11:49,030 --> 00:11:46,959
which was a part of a

308
00:11:50,150 --> 00:11:49,040
grant program called program exploration

309
00:11:53,110 --> 00:11:50,160
france which allowed

310
00:11:54,470 --> 00:11:53,120
a research travel grant to visit a

311
00:11:57,350 --> 00:11:54,480
collaborators

312
00:11:58,870 --> 00:11:57,360
research lab in paris so thank you very

313
00:12:00,870 --> 00:11:58,880

much for your time and attention

314
00:12:02,870 --> 00:12:00,880
i'm very happy to take any questions any

315
00:12:03,829 --> 00:12:02,880
time and please feel free to contact me

316
00:12:05,910 --> 00:12:03,839
by email