
AbSciCon
2019

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

2
00:00:12,650 --> 00:00:09,160
[Applause]

3
00:00:15,709 --> 00:00:12,660
hi my name is Qashqai fukushima from LC

4
00:00:18,769 --> 00:00:15,719
and today i would like to explain about

5
00:00:22,010 --> 00:00:18,779
the ongoing new tech the technological

6
00:00:24,710 --> 00:00:22,020
method that we've been investigating to

7
00:00:26,630 --> 00:00:24,720
prove the surface to prove the peptide

8
00:00:30,790 --> 00:00:26,640
basically a random peptide sequence

9
00:00:35,750 --> 00:00:30,800
space using absorption type technology

10
00:00:37,820 --> 00:00:35,760
so many of us know that we still don't

11
00:00:40,010 --> 00:00:37,830
know where the origin of fly where life

12
00:00:44,330 --> 00:00:40,020
actually originated but one thing that

13
00:00:47,930 --> 00:00:44,340

we know is that from the inorganic

14
00:00:50,889 --> 00:00:47,940
organic compounds some hell through the

15
00:00:53,540 --> 00:00:50,899
evolution of these chemical molecules

16
00:00:55,910 --> 00:00:53,550
they eventually led to the emergence of

17
00:00:58,340 --> 00:00:55,920
the polymers so there should have been a

18
00:01:00,529 --> 00:00:58,350
state where a stage where a body

19
00:01:02,689 --> 00:01:00,539
polymers were formed through many

20
00:01:07,090 --> 00:01:02,699
different types of processes like drive

21
00:01:10,070 --> 00:01:07,100
at cycle diagenesis impact shock heating

22
00:01:11,930 --> 00:01:10,080
hydrothermal reactor so many places on

23
00:01:13,339 --> 00:01:11,940
so many different planetary bodies could

24
00:01:13,580 --> 00:01:13,349
take this type of reaction could take

25
00:01:17,120 --> 00:01:13,590
place

26
00:01:19,600 --> 00:01:17,130
and among those abiotic polymers there

27
00:01:22,940 --> 00:01:19,610
should have been some sort of selection

28
00:01:25,550 --> 00:01:22,950
selective process that led to eventually

29
00:01:27,199 --> 00:01:25,560
led to a functional polymer here I'm not

30
00:01:30,740 --> 00:01:27,209
talking about the replication of

31
00:01:33,650 --> 00:01:30,750
polymers it's even prior to that what is

32
00:01:36,770 --> 00:01:33,660
the first filter or the selection that

33
00:01:38,570 --> 00:01:36,780
could have taken place and my answer to

34
00:01:41,270 --> 00:01:38,580
that is the mineral surface absorption

35
00:01:43,460 --> 00:01:41,280
so especially focusing on the earlier

36
00:01:44,150 --> 00:01:43,470
Earth what sort of minerals were

37
00:01:46,249 --> 00:01:44,160
abundant

38
00:01:49,580 --> 00:01:46,259

one of the major minerals that we can

39
00:01:52,809 --> 00:01:49,590
think of is the iron sulphides so here

40
00:01:55,219 --> 00:01:52,819
the elements on the left you see the

41
00:01:58,370 --> 00:01:55,229
abundant elements for example iron and

42
00:02:00,800 --> 00:01:58,380
software both abundant on kadian archaea

43
00:02:02,809 --> 00:02:00,810
notion and you can see these two

44
00:02:04,999 --> 00:02:02,819
different types of iron sulfide minerals

45
00:02:09,139 --> 00:02:05,009
that must have been existed on early

46
00:02:10,940 --> 00:02:09,149
Earth and sorry it's not intentional but

47
00:02:13,130 --> 00:02:10,950
somehow the resolution is very bad but

48
00:02:15,080 --> 00:02:13,140
here there this paper is actually

49
00:02:17,360 --> 00:02:15,090
explaining about there could have been a

50
00:02:19,580 --> 00:02:17,370
progression of iron sulfur cluster from

51
00:02:20,870 --> 00:02:19,590
these hydrothermal system to eventually

52
00:02:23,390 --> 00:02:20,880
lead to the biological protein

53
00:02:27,500 --> 00:02:23,400
so here I'm focusing on the iron

54
00:02:30,470 --> 00:02:27,510
sulphides and by using a random peptide

55
00:02:34,520 --> 00:02:30,480
sequence so this is basically it's a

56
00:02:37,490 --> 00:02:34,530
octamer which has one fixed tyrosine on

57
00:02:40,160 --> 00:02:37,500
the n-terminal with following by seven

58
00:02:42,230 --> 00:02:40,170
random any amino acid residues consisted

59
00:02:43,880 --> 00:02:42,240
five different types of amino acids so

60
00:02:47,840 --> 00:02:43,890
it's a combination of five to the power

61
00:02:50,090 --> 00:02:47,850
of seven and once you subject this

62
00:02:53,000 --> 00:02:50,100
random peptide onto the surface of the

63
00:02:55,330 --> 00:02:53,010

iron sulfide mineral you can then wash

64
00:02:57,740 --> 00:02:55,340
off all the nonspecific binders and

65
00:03:00,170 --> 00:02:57,750
simply analyze the ones that are

66
00:03:02,900 --> 00:03:00,180
remaining on the surface and in order to

67
00:03:05,290 --> 00:03:02,910
do so we're using this off technique

68
00:03:07,910 --> 00:03:05,300
called mal D ms/ms

69
00:03:10,910 --> 00:03:07,920
the one of the reason is because we want

70
00:03:12,380 --> 00:03:10,920
to know the mass of the peptides that

71
00:03:14,600 --> 00:03:12,390
are remaining but also at the same time

72
00:03:17,180 --> 00:03:14,610
we want to fragment these peptides and

73
00:03:20,300 --> 00:03:17,190
go into the sequence level so the two

74
00:03:22,100 --> 00:03:20,310
key questions one is well iron sulphide

75
00:03:24,890 --> 00:03:22,110
surface absorption can lead to amino

76
00:03:28,130 --> 00:03:24,900
acid compositional bias of the peptides

77
00:03:31,100 --> 00:03:28,140
and second whether there is any sequence

78
00:03:33,530 --> 00:03:31,110
specificity that can emerge to do this

79
00:03:37,160 --> 00:03:33,540
processes and one of the interesting

80
00:03:39,350 --> 00:03:37,170
intriguing fact is that the biology as

81
00:03:42,110 --> 00:03:39,360
we know we're actually using iron sulfur

82
00:03:45,110 --> 00:03:42,120
cluster which actually surrounded by

83
00:03:47,990 --> 00:03:45,120
either cysteine or histidine in the

84
00:03:49,760 --> 00:03:48,000
first shell most adjacent to these

85
00:03:51,410 --> 00:03:49,770
aren't sulfur's so you could imagine

86
00:03:54,530 --> 00:03:51,420
these amino acids should have

87
00:03:56,360 --> 00:03:54,540
contributed significantly in order to

88
00:03:58,520 --> 00:03:56,370

maintain these are and sulfur clusters

89
00:04:03,880 --> 00:03:58,530
so that's why I included these two amino

90
00:04:06,440 --> 00:04:03,890
acids in the random amino acid pool so

91
00:04:09,230 --> 00:04:06,450
well so you can think of there's gonna

92
00:04:13,760 --> 00:04:09,240
be 338 different isomers with different

93
00:04:16,310 --> 00:04:13,770
molecular weights containing 78,000 125

94
00:04:18,740 --> 00:04:16,320
unique sequences so for example if you

95
00:04:22,310 --> 00:04:18,750
focus on one isomer pool so say

96
00:04:25,250 --> 00:04:22,320
molecular weight of 769 you can have 208

97
00:04:27,410 --> 00:04:25,260
different types of isomer sequences so

98
00:04:30,260 --> 00:04:27,420
what I did here is that I started off by

99
00:04:31,930 --> 00:04:30,270
making an amorphous iron sulfide mineral

100
00:04:34,840 --> 00:04:31,940
mixing iron chloride

101
00:04:37,900 --> 00:04:34,850
and a sodium sulfide precipitating out

102
00:04:40,240 --> 00:04:37,910
this iron sulfide amorphous mixing these

103
00:04:43,000 --> 00:04:40,250
random peptides into that and then

104
00:04:45,370 --> 00:04:43,010
rinsing again and again to remove all

105
00:04:48,000 --> 00:04:45,380
the nonspecific binders and eventually

106
00:04:52,810 --> 00:04:48,010
analyzing the absorbed peptides directly

107
00:04:54,790 --> 00:04:52,820
using the MALDI so on the left is iron

108
00:04:56,980 --> 00:04:54,800
sulphide without peptide but once you

109
00:04:58,510 --> 00:04:56,990
add the peptide what happens is that you

110
00:05:00,400 --> 00:04:58,520
start seeing these clumps of iron

111
00:05:03,370 --> 00:05:00,410
sulfide mineral meaning that the peptide

112
00:05:07,030 --> 00:05:03,380
is starting to stick to each perhaps

113
00:05:11,890 --> 00:05:07,040

peptide is working as like a glue to in

114
00:05:14,850 --> 00:05:11,900
order to form these gigantic large

115
00:05:17,500 --> 00:05:14,860
particles so here the average size

116
00:05:20,080 --> 00:05:17,510
nanoparticle is from nanometer order to

117
00:05:23,380 --> 00:05:20,090
micron or scale but here you can

118
00:05:25,030 --> 00:05:23,390
actually visualize it in your eyes so

119
00:05:27,940 --> 00:05:25,040
melp so for the people who don't know

120
00:05:29,260 --> 00:05:27,950
that the technology of Mally I'll just

121
00:05:30,370 --> 00:05:29,270
go through this briefly but it's called

122
00:05:33,490 --> 00:05:30,380
matrix assisted laser desorption

123
00:05:35,980 --> 00:05:33,500
ionization mass spec so you mix your

124
00:05:41,080 --> 00:05:35,990
peptide with the so called matrix which

125
00:05:43,540 --> 00:05:41,090
allows protonation of the peptide and by

126
00:05:46,300 --> 00:05:43,550
hitting with a laser it has a specific

127
00:05:48,760 --> 00:05:46,310
absorbance so if serves the light energy

128
00:05:50,890 --> 00:05:48,770
and then it on eise's the peptide and

129
00:05:54,670 --> 00:05:50,900
the peptides will subject it to the

130
00:05:56,290 --> 00:05:54,680
time-of-flight aspect so here's the our

131
00:05:59,290 --> 00:05:56,300
first planet luminary results of

132
00:06:02,110 --> 00:05:59,300
analyzing both the the random peptide

133
00:06:04,210 --> 00:06:02,120
and the peptides are after absorbed on

134
00:06:09,070 --> 00:06:04,220
the mineral surface so you can actually

135
00:06:10,810 --> 00:06:09,080
see well it's very messy but still you

136
00:06:13,060 --> 00:06:10,820
can actually see the difference that's

137
00:06:16,270 --> 00:06:13,070
it slightly shifted towards the right so

138
00:06:19,000 --> 00:06:16,280

it seems like slightly heavier peptide

139
00:06:20,470 --> 00:06:19,010
molecules are started to select and also

140
00:06:22,720 --> 00:06:20,480
you can see that there are less noise

141
00:06:24,790 --> 00:06:22,730
noisy here meaning that many of the

142
00:06:26,890 --> 00:06:24,800
peptide should have been rinsed off but

143
00:06:28,600 --> 00:06:26,900
some of them are still remaining so

144
00:06:31,360 --> 00:06:28,610
let's go into the let's look into what's

145
00:06:34,540 --> 00:06:31,370
happening so here what I did was I

146
00:06:38,200 --> 00:06:34,550
plotted all the older peptides their

147
00:06:40,300 --> 00:06:38,210
peak area normalized peak area to the

148
00:06:42,040 --> 00:06:40,310
absorbed peptide peak areas so what you

149
00:06:45,340 --> 00:06:42,050
can see is that there's almost no

150
00:06:48,190 --> 00:06:45,350
correlation so it's only like art

151
00:06:50,710 --> 00:06:48,200
the correlation coefficient is 0.43

152
00:06:52,900 --> 00:06:50,720
meaning that many of these peptides are

153
00:06:54,910 --> 00:06:52,910
not following the profile of the

154
00:06:58,120 --> 00:06:54,920
original peptide that I have subjected

155
00:07:00,130 --> 00:06:58,130
on the right is the supernatant so if

156
00:07:03,490 --> 00:07:00,140
you wash off most of the peptides those

157
00:07:05,590 --> 00:07:03,500
peptides actually follow the same

158
00:07:07,330 --> 00:07:05,600
profile of the peptides that I used it

159
00:07:09,100 --> 00:07:07,340
initially so that means there's

160
00:07:11,980 --> 00:07:09,110
something the some sort of selection

161
00:07:15,520 --> 00:07:11,990
happening already against a mineral

162
00:07:19,030 --> 00:07:15,530
bound peptides and just in case that

163
00:07:21,280 --> 00:07:19,040

these profile bias is not coming from

164
00:07:24,400 --> 00:07:21,290
the oxidation of the thigh or group of

165
00:07:26,980 --> 00:07:24,410
sustain I did with him without the

166
00:07:29,350 --> 00:07:26,990
reductant the t set just to make sure

167
00:07:31,960 --> 00:07:29,360
that the cysteine is not converting to

168
00:07:35,620 --> 00:07:31,970
cysteine or forming some weird sustained

169
00:07:37,780 --> 00:07:35,630
sustained bond duplex peptide so it sits

170
00:07:39,850 --> 00:07:37,790
nicely correlated here that means the

171
00:07:42,400 --> 00:07:39,860
cysteine is already the sister thyroid

172
00:07:45,300 --> 00:07:42,410
group is reduced so that means we can

173
00:07:47,980 --> 00:07:45,310
now consider that the peptide is

174
00:07:50,230 --> 00:07:47,990
absorbed on the surface and the sister

175
00:07:54,700 --> 00:07:50,240
at the thyroid group is still there to

176
00:07:56,740 --> 00:07:54,710
do the job however when I looked at what

177
00:07:59,080 --> 00:07:56,750
type of peptides are absorbed on the

178
00:08:02,140 --> 00:07:59,090
iron sulfide surface there were there

179
00:08:04,570 --> 00:08:02,150
was a clear tendency towards Hyken a

180
00:08:08,050 --> 00:08:04,580
component hi a composition of histidine

181
00:08:10,060 --> 00:08:08,060
so you can see these are all one

182
00:08:12,550 --> 00:08:10,070
histidine bearing peptides to histidine

183
00:08:15,010 --> 00:08:12,560
bearing peptides three four five and six

184
00:08:19,030 --> 00:08:15,020
so you can actually see the trends going

185
00:08:20,320 --> 00:08:19,040
up although even within these like to

186
00:08:23,940 --> 00:08:20,330
histidine bearing three history and

187
00:08:26,590 --> 00:08:23,950
bearing there our composition or bias

188
00:08:27,880 --> 00:08:26,600

the intensity is different among these

189
00:08:30,850 --> 00:08:27,890
different peptides but there are these

190
00:08:33,280 --> 00:08:30,860
overall trends whereas it was kind of

191
00:08:36,010 --> 00:08:33,290
disappointing to see that if you now

192
00:08:39,250 --> 00:08:36,020
focus on cysteine containing peptide but

193
00:08:40,959 --> 00:08:39,260
without the histidine there's no trend

194
00:08:46,470 --> 00:08:40,969
so that means histidine is the major

195
00:08:48,780 --> 00:08:46,480
contributor and sustain is not so

196
00:08:49,960 --> 00:08:48,790
finally I would like to go into the

197
00:08:53,380 --> 00:08:49,970
ms/ms

198
00:08:56,710 --> 00:08:53,390
a process so this process easier is to

199
00:08:59,230 --> 00:08:56,720
basically cut the peptide bond of a

200
00:09:01,960 --> 00:08:59,240
specific peak so you can pick a peak

201
00:09:04,060 --> 00:09:01,970
do the ms/ms and see what's of a peptide

202
00:09:08,199 --> 00:09:04,070
fragment you can get out of these Peaks

203
00:09:13,540 --> 00:09:08,209
and if you do that against for example a

204
00:09:16,030 --> 00:09:13,550
135 mm / z which should contain 140

205
00:09:18,160 --> 00:09:16,040
different isomer with this composition

206
00:09:20,769 --> 00:09:18,170
of amino acids you end up getting these

207
00:09:22,389 --> 00:09:20,779
three major peptides so if you look at

208
00:09:25,120 --> 00:09:22,399
these major peptides that are detected

209
00:09:25,920 --> 00:09:25,130
they all Harbor histidine at the

210
00:09:29,230 --> 00:09:25,930
c-terminus

211
00:09:31,000 --> 00:09:29,240
one adjacent to the first tyrosine and

212
00:09:33,010 --> 00:09:31,010
then there are 2 histidines in the

213
00:09:36,100 --> 00:09:33,020

middle and there seems to be some sort

214
00:09:38,290 --> 00:09:36,110
of a pattern here starting to emerge the

215
00:09:41,370 --> 00:09:38,300
same thing feature was also found in

216
00:09:45,100 --> 00:09:41,380
when I when we did the MSM s against 881

217
00:09:48,400 --> 00:09:45,110
which contains 420 different isomer

218
00:09:50,110 --> 00:09:48,410
but then narrowing down to 3 we still

219
00:09:52,810 --> 00:09:50,120
haven't finished detecting all the peaks

220
00:09:55,180 --> 00:09:52,820
yet but even though when we look at

221
00:09:57,370 --> 00:09:55,190
these first three that are most major we

222
00:09:59,470 --> 00:09:57,380
also see the same pattern having the

223
00:10:02,139 --> 00:09:59,480
histidine on the C terminus and now

224
00:10:03,850 --> 00:10:02,149
replacing the center with the cysteine

225
00:10:06,400 --> 00:10:03,860
so you have the cysteine is always

226
00:10:08,110 --> 00:10:06,410
consistent showing up in this region now

227
00:10:09,000 --> 00:10:08,120
what do we see from what do we learn

228
00:10:11,980 --> 00:10:09,010
from this

229
00:10:13,660 --> 00:10:11,990
so actually what biology is doing is

230
00:10:18,430 --> 00:10:13,670
when you look at the iron sulfur cluster

231
00:10:21,160 --> 00:10:18,440
protein the c XX c or c xh or c XX h

232
00:10:24,069 --> 00:10:21,170
motif always appears so it seems like

233
00:10:26,519 --> 00:10:24,079
the coordination that biology uses to

234
00:10:29,980 --> 00:10:26,529
actually capture the iron sulphides

235
00:10:32,199 --> 00:10:29,990
actually does seem to work or at least

236
00:10:34,870 --> 00:10:32,209
enhance enriched in these iron sulfide

237
00:10:37,780 --> 00:10:34,880
mineral absorbed peptides so here are

238
00:10:39,550 --> 00:10:37,790

the conclusions so we did the mal DMS

239
00:10:42,490 --> 00:10:39,560
type approach in order to probe the

240
00:10:44,170 --> 00:10:42,500
sequence types in sequence space of the

241
00:10:46,420 --> 00:10:44,180
peptides are specific to certain types

242
00:10:49,600 --> 00:10:46,430
of minerals and histidine seems to be

243
00:10:52,480 --> 00:10:49,610
the most prominent amino acids that are

244
00:10:54,040 --> 00:10:52,490
found in the absorbed peptides no trend

245
00:10:56,800 --> 00:10:54,050
was found from in the sustain and

246
00:10:58,810 --> 00:10:56,810
composition however when we look at the

247
00:11:00,460 --> 00:10:58,820
sequence level we start to see these

248
00:11:02,230 --> 00:11:00,470
cysteine residues showing up in a

249
00:11:03,940 --> 00:11:02,240
specific position so that's something

250
00:11:06,790 --> 00:11:03,950
that we need to understand even further

251
00:11:08,530 --> 00:11:06,800
and so for the future work we can try

252
00:11:11,079 --> 00:11:08,540
the histidine negative random peptides

253
00:11:12,879 --> 00:11:11,089
just to see maybe the surface is already

254
00:11:14,739 --> 00:11:12,889
coded by the histidine containing

255
00:11:16,479 --> 00:11:14,749
dice so what happens if we remove all

256
00:11:18,189 --> 00:11:16,489
those cans cysteines start to become

257
00:11:20,679 --> 00:11:18,199
dominant that's something that we want

258
00:11:22,689 --> 00:11:20,689
to understand the other is using sulfur

259
00:11:24,879 --> 00:11:22,699
bake vacant pyrite surface there's been

260
00:11:27,160 --> 00:11:24,889
studies showing that the sulfur vacant

261
00:11:29,499 --> 00:11:27,170
surface of an iron sulfide can actually

262
00:11:32,019 --> 00:11:29,509
absorb cysteine so maybe that's another

263
00:11:34,150 --> 00:11:32,029

factor that we need to think about

264
00:11:36,069 --> 00:11:34,160
consider and with that I would like to

265
00:11:39,489 --> 00:11:36,079
thank all my collaborators Christine

266
00:11:41,710 --> 00:11:39,499
Johnson from LC that I saw was also from

267
00:11:44,849 --> 00:11:41,720
LC but recently moved to gem stack

268
00:11:49,509 --> 00:11:44,859
ksama song is he's a great mass spec

269
00:11:51,099 --> 00:11:49,519
person he's a master of mass spec but he

270
00:11:54,340 --> 00:11:51,109
recently moved to this lab that makes

271
00:11:56,530 --> 00:11:54,350
the peptide so we're in good shape and

272
00:12:04,199 --> 00:11:56,540
with that I would like to thank my

273
00:12:12,150 --> 00:12:06,729
great thank you very much we have time

274
00:12:22,479 --> 00:12:12,160
for one question and let's go with the

275
00:12:24,100 --> 00:12:22,489
yes only one pick one that's a very good

276
00:12:26,470 --> 00:12:24,110
question but well I think what will

277
00:12:28,299 --> 00:12:26,480
happen is peptide will win against amino

278
00:12:31,409 --> 00:12:28,309
acids so if you compare a single mean

279
00:12:33,909 --> 00:12:31,419
ASUS to a dipeptidyl tripeptide

280
00:12:36,669 --> 00:12:33,919
typically the longer the peptide is the

281
00:12:39,309 --> 00:12:36,679
more stronger they bound to the surface

282
00:12:41,590 --> 00:12:39,319
so that means the free energy have sorry

283
00:12:44,229 --> 00:12:41,600
the free mean acid have no chance but I

284
00:12:46,859 --> 00:12:44,239
haven't tested mixing for example two

285
00:12:48,789 --> 00:12:46,869
different chain lengths polymer and

286
00:12:51,369 --> 00:12:48,799
maybe that's an interesting way to

287
00:12:52,720 --> 00:12:51,379
actually look at whether longer peptide

288
00:12:56,169 --> 00:12:52,730

can actually win against the others

289
00:12:57,040 --> 00:12:56,179
thank you all right thank you very much