E.colid-State Drive

NOTE

> All the content is writed by Markdwon you can see the source in my Github there store my class notes but not all.

Table of Content

Introduction

The Motivation to Study this topic

At first I have to explan why choose this topic. In the last assignment the assistant who comment my homework said " 可挑選有點難度的文章" in the field "文章深度適切".It piss me off when I saw it. And that assignment take me five nights from 8pm to 2am to understand the article and to finish the assignment.So this time I pick this topic maybe it's more difficult than last time.

E.coli

E.coli (Escherichia coli) is the commonest microbe in animal's body.
Besides made human get stomachache, E.coli also bring some contribution for human due to their *genome is easy to edit .*

DNA

DNA has been described as the most ultimate infomation storage.It can use four bases ACTG to store large of information.And also it is the *lightest* way to store infomation.
The size of human's DNA is 3.2Gbp, lets convert it into computer unit.

The base unit of DNA is *base pair (bp)* and it is combined by 2 *nucleobases.* Computer's base unit is bit but we usually use byte(8bit) as a base storage unit. There are 2 base in a base pair so we can know 4 bp is equivalent to 1 byte.

$$3.2Gbp = 3.2 \times 10^9 bp = 3.2 \div 4 \times 10^9 bp = (0.8 \times 10^9) bytes = (8 \times 10^8) bytes$$
$$Convert\ to\ MB \Rightarrow 8 \times 10^8 bytes = (\frac{8 \times 10^8}{1024^2}) bytes \Rightarrow 762.939453125 MB$$

As we can see a human we need 763 MB to store in computer. what's that means?

It means we need the area equivalent to a 1Gb NAND chip (the area of NAND chip we use now is close to $3cm^2$) to store a humanrace's DNA.

Keywords:

- E.coli (Escherichia coli)
- genome is easy to edit
- base pair (bp)
- nucleobases

Key Point:

> DNA is a more smaller and lighter information container. If we want to store a human's genome, we can use chip but it take larger place then DNA

Storage

Scientists have already used plain old DNA to encode and store all 587287 words of *War and Peace*,a list of all the plant material archived in the Svalbard Seed Vault, and an OK Go music video.

But now scientists created a living library,embedded whitin,you guessed it: E.coli.

Harvard researchers describe using *Crispr system* to insert bits of DNA encoded with photos and GIF of a galloping horse into live bacteria.And they have retrieved and reconstructed the images by sequencing the bacterial genomes,the images got about 90 percent accuracy

Keywords:

Crispr System

Key Point:

> Scientists have store digital data into E.coli's DNA and also retrived, reconstructed successful by Crispr.

Crispr

CRISPR (**C**lustered **R**egularly **I**nterspaced **S**hort **P**alindromic **R**epeats) makes all shorts of wild things possible and people are rightfully excited about it. As a very short prime, CRISPR-associated proteins(in this instance, specifically proteins known as Cas1 and Cas2) act as a DNA version of a computer's Ctrl+X tool, allowing scientists to select specific segments of DNA, cut them out, fiddle with the, and even replace them altogether.

Key words:

- Cas1
- Cas2

Key Point:

> Crispr is a technique to edit DNA, it can paste or cut out a segment of gene and made the genome turn into the shape scientists want. So here we can use this technique to write, read a data from DNA.Also thie technique is wildly using in medical field.

Principle

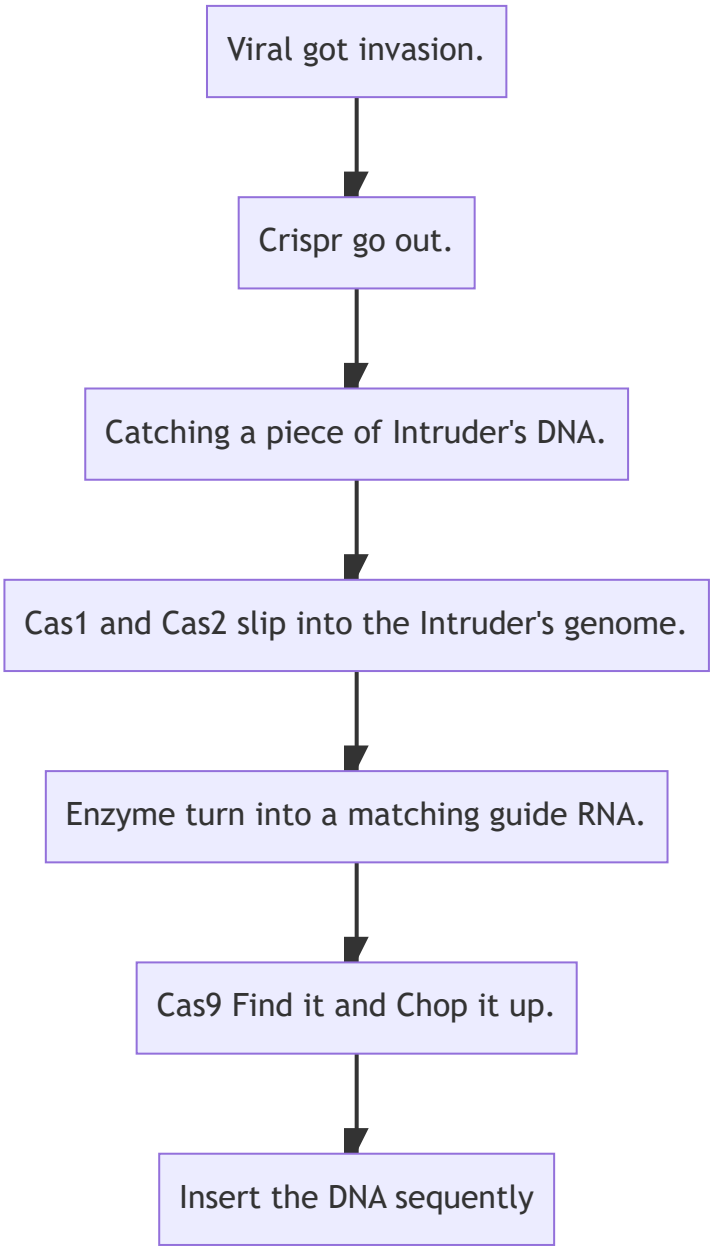
In this case maybe you are confuse what is Crispr-Cas1 and Cas2? And what's the difference between Crispr-Cas9 and Cas1, Cas2?

Crispr-Cas9 is the protein that does all the cutting,i.e. gene editing's heavy lifting. Lesser known are Cas1 and Cas2. They are the ones that tell Cas9 where to do the cutting.

The whole process that Crispr works is when enemy injecting its DNA into an E.coli's cell, The Crispr in E.coli will go out and try to catch the enemy's DNA, Also the Cas1 and Cas2 will slip into the enemy's genome to marking the segment, the enzyme will turn the genome segment into a matching guide RNA, then Cas9 will find it and chop it up.

Finally the genome will be inserted into the E.coli's genome in a specific space. And the sequence is not sorted by random, It's sorted by the time that the enemy's DNA invasion.

If we watch a bacteria's DNA, we'll find the history that this bacteria's defense. If above is too hard to understand you can see the chart following.



key words

- Crispr-Cas9

key point

> This chapter is talking about how the Crispr system works. And we can know about that the system is a bacteria's defense system. So we use the mechanism to insert the data what we want to store.

Appliction

This technology is not for store digital data mainly, though this is a bonus. This technology is not only for scaling down our computer hard drive to a bacterial size, but also to store our gene information on a bacteria, through its machanism to record any animal's cell, made it into a biological information recoder.

key words

- Biological information recoder

key point

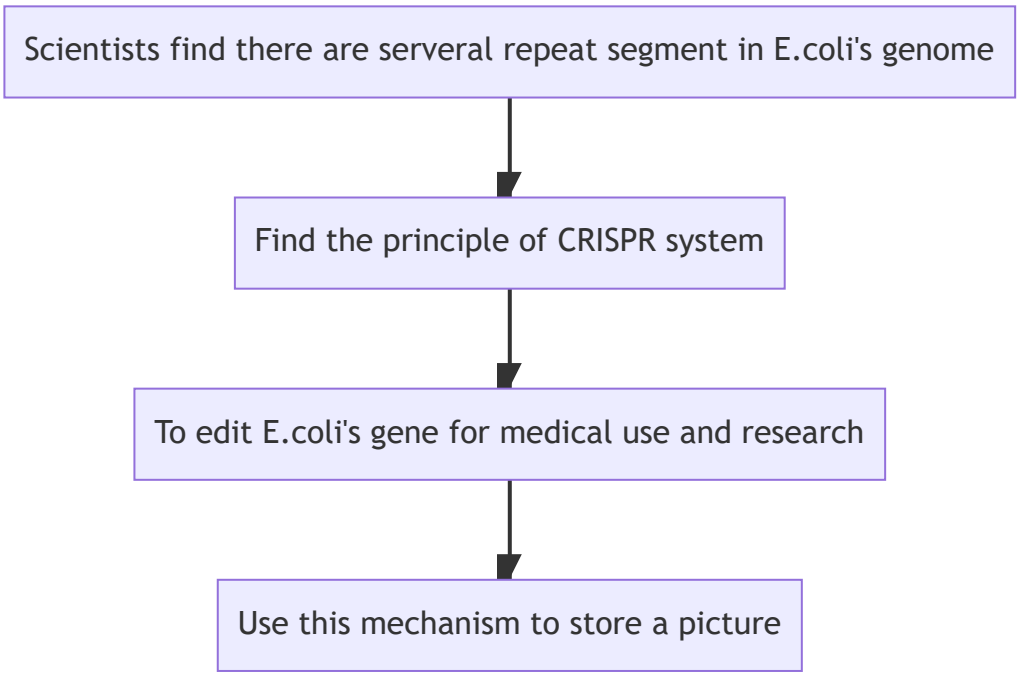
> Through the CRISPR system we can made bacteria into a biological information recorder.It made us use less space to store more information. And it's more safe than our drive because bacteria copy itself just use a few minutes but drive maybe need many hours, and we can freeze a bateria that its DNA will save for several years, but hard drive not, if you cut out power for serveral years maybe the data will disappearing and you never gonna made it back.

Conclusion（ Note ）

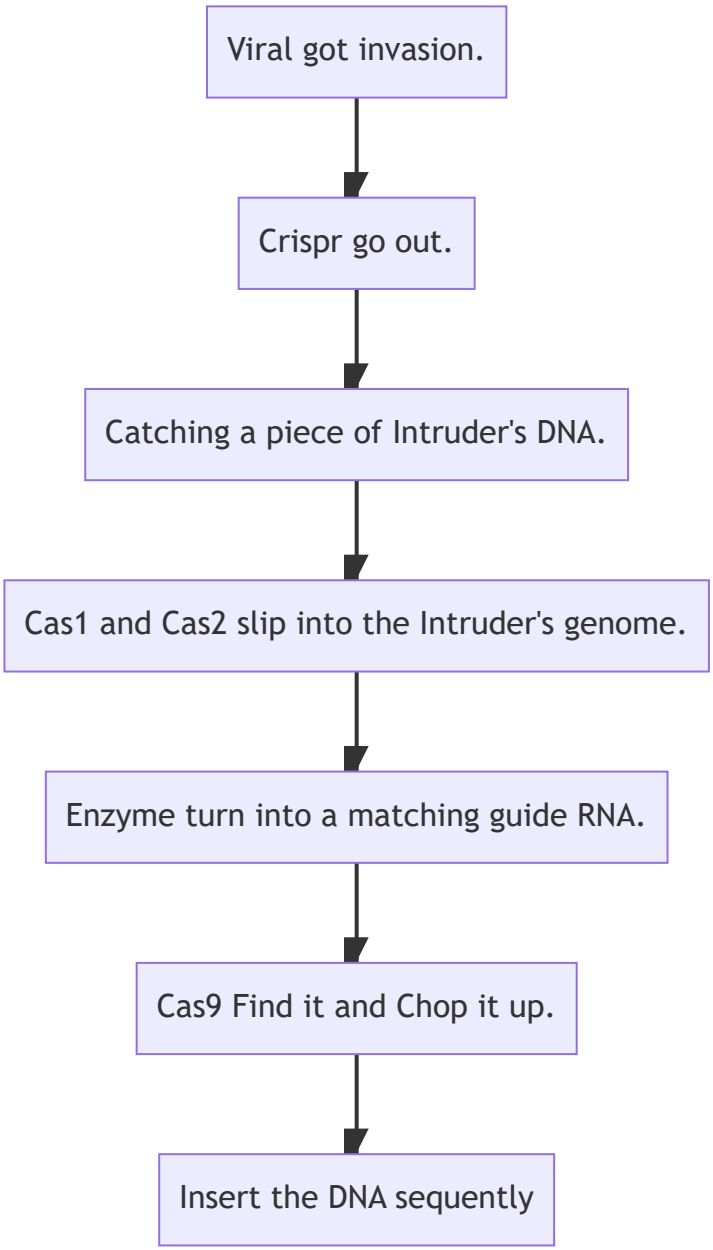
E.Coli is a bacteria that is easy to edit, so we can use this bacteria to store our data. And we can use the Crispr system to edit the E.coli's genome, so we can store our data into the E.coli's genome. And we can use the Crispr system to retrieve the data from the E.coli's genome. And we can use the Crispr system to reconstruct the data from the E.coli's genome. And we can use the Crispr system to edit the E.coli's genome to make it into a biological information recorder.

Concept map

History


Scientists find there are serveral repeat segment in E.coli's genome
Find the principle of CRISPR system
To edit E.coli's gene for medical use and research
Use this mechanism to store a picture

Principle :


Viral got invasion.
Crispr go out.
Catching a piece of Intruder's DNA.
Cas1 and Cas2 slip into the Intruder's genome.
Enzyme turn into a matching guide RNA.
Cas9 Find it and Chop it up.
Insert the DNA sequently

Study sheet

本圖感謝漳和國中Su-Huei Chang老師同意使用
下圖小貓來自 https://www.pinclipart.com/downpngs/iTmRxxo_funny-black-cat-clipart-public-domain-free-clipart/

Article Source

Scientists have inserted a GIF of a horse into living bacteria — did your brain just explode?

Gif and image written into the DNA of bacteria

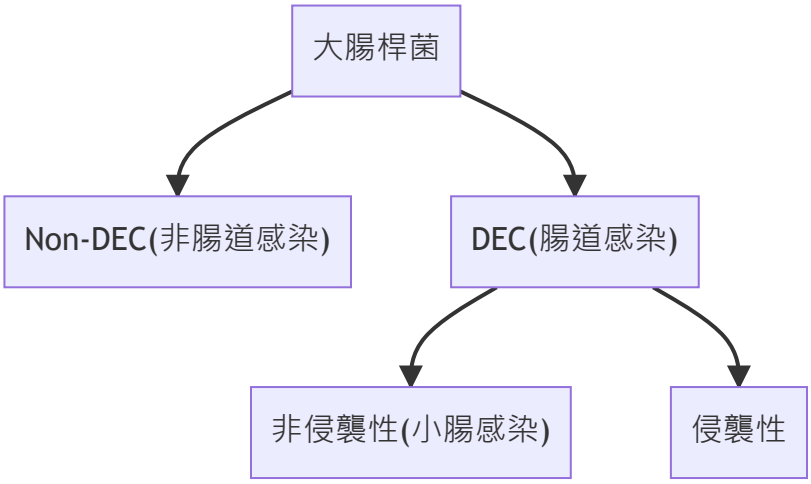
Scientists Upload a Galloping Horse GIF Into Bacteria With Crispr

Reference

- 基因組學 - 人類基因體計劃及其應用
- Base pair
- Cas1
- Cas2
- Introduction to the CRISPR/Cas9 system

Class Note

大腸桿菌(E.coli)埃西氏菌屬(Escherichia)



基本介紹

- 生化特徵IMViC-> ++-- :吲哚(indole)反映、MV(MR-VP;Methyl red甲基紅，Voges-Proskauer)、Citrate檸檬酸鹽
- 感染：大多數感染是**內源性**的
- 預防、治療和控制
  - 正確烹飪牛肉產品以降低EHEC感染的風險。
  - 保持高衛生標準，以降低暴露的風險。
  - 對不威脅生命的感染，一般都支持性治療。抗生素使用需參考體外藥敏感試驗結果。

```
IMViC -> ++--
indole(+)
Methyl red(+)
Voges(-)
Citrate(-)

- indole:分解色胺酸的產物
- 產生很多酸的話會使甲基紅變色
```

非腸道感染

- UPEC(尿道致病性大腸桿菌,Uropathogenic E.coli)
  - 黏附素：PAP菌毛(腎盂腎炎相關菌毛,pyelonephriti associated pi)
- NMEC(新生兒撓膜炎大腸桿菌,Neonatal meningitis E.coli)

- 莢膜K1

腸道感染

非侵襲性

Watery diarrhea 吸附素與分泌性毒素為媒介

- ETEC 腸產毒性大腸桿菌 Enterotoxigenic
  - 吸附素：CFA
  - 毒素：ST、LT
- EAEC 腸聚集性大腸桿菌 Enteroaggregative
  - 吸附素：生物膜
  - 毒素：EAST

```
Entero--- 腸道---
---toxigenic ---產毒素的
---aggregative ---聚集的
```

侵襲性

- EHEC腸出血性大腸桿菌 Enterohemorrhagic
  - O157H7;牛肉;HUS Sorbitol MAC(-)(Sorbital不分解)
    - 吸附素：非菌毛黏附素
    - 毒素：類志賀毒素Stx
- EPEC 腸致病性大腸桿菌 Enteropathogenic
  - 吸附素：
  - 質體：BFP
  - 致病島：Intimin,Tur,T3SS-A/E
- EIEC 腸侵襲性大腸桿菌 Enteroinvasive
  - 吸附：非菌毛黏附素T3SS，類似Listeria

大腸桿菌共通點

- 吸附素：Type 1 pili (common pili) : 結合甘露糖
- 毒素：Endotoxin
- 侵襲素：Enterochelin (iron chelator)

克雷伯菌屬(Klebsiella)

- 不運動，有多糖莢膜運動，菌落成黏稠狀
- 肺炎克雷伯菌(K.pneumoniae)是主要的分離株
  - 對免疫衰弱者可引起大葉性肺炎，特徵為鐵鏽色的痰
  - 在台灣：肝膿腫通常鑑於肺炎克雷伯氏菌感染。

志賀氏菌屬(Shigella)(Biogroup of E.coli)

- 特點
  - 根據DNA，為E.coli菌種的biotype
  - 根據O抗原，分A到D群四血清型，毒力由強而弱
    - S.dysenteriae(A型),S.flexneri(B型),S.boydii(C型),S.sonnei(D型)
- 毒力因子：黏附、侵襲、細胞內複製和內外毒素
  - 志賀毒素是一種A-B毒素，外毒素A切割28S rRN，抑制蛋白質合成，損傷腎小管內皮細胞，導致溶血尿毒症綜合徵hemolytic uremic syndrome,HUS
- 致病性：所有物種都會引起細菌性痢疾(Shigellosis)
  - 侵襲性，侵犯大腸回腸末端造成年末壞死，少侵入血流，很少引起腸道外的感染。
    - 症狀為發燒，腹部絞痛、腹瀉、黏液性血便
  - 併發症：溶血性結腸炎(Hemolytic colitis,HC)、溶血性尿毒症綜合徵、反應性關節炎(Reactive arthritis)
- 流行病學
  - 具高度傳染性(10-100cfu即造成感染->acid resistance(耐酸))
    - 感染劑量低
  - 人類為唯一儲存宿主
  - 疾病通過糞口途徑，在人與人之間傳播
  - 疾病風險最高的患者是日托中心，托兒所和監護機構的幼兒及其家人；男同性戀
- 預防與治療
  - 因其具高度感染性，應採取適當的感染控制措施。
  - 補充水分
  - 抗生素治療可縮短糞便排放菌體期間及縮短病程
  - 但因為抗藥性的風險，對非嚴重患者使用抗生素治療是個問題
-

重點

```
- 不運動
- No Flegalla(無鞭毛)<span class="yellow">生化反應傾向惰性</span>
- glicose(+)
- oxidase(-)
- IMViC:++--
```

補充

-osis : OOO病

沙門氏菌屬(Salmonella)

- 特點
  - 為化學異營性，大部分菌種產生H_2S
  - 根據DNA，人類主要致病菌為S.enterica一個種，以下再分六個亞種
  - 血清型可分為

類型	內容
傷寒血清型	• 只能在人與人 • 侵襲性，導致傷寒，副傷寒。 • 侵入性的病需要立即用抗生素治療
非傷寒血清型	• 可以從動物(禽類等)傳染給人和人與人之間傳染 • 大部分為非侵襲性的，僅感染腸胃道導致沙門氏菌腸炎或食物中毒，不須抗生素即可緩解症狀

引起疾病

- 無症狀定植
  - 無症狀慢性攜帶者(1%-5%的患者)細菌在膽囊和膽道中持續超過一年。
  - Vi抗體出現高效價為帶菌者
- 腸炎，定植性感染
- 菌血症，侵襲性感染
- 傷寒或腸熱病(Typhoid and enteric fever)
  - 當沙門氏菌侵入血流而遍佈全身，出現玫瑰疹(Rose spot)並分泌內毒素，導致敗血症，將導致危及生命的低血容量性和感染性休克，需要抗生素等地重症監護。
  - 10%的患者可能有局部化膿性感染，例如骨髓炎，心內膜炎，關節炎等。
- 流行病學、預防與治療
  - 傷寒血清型抗生素治療至關重要
    - 未使用抗生素，死亡率為10-15%
  - 非傷寒型不推薦使用抗生素治療
    - 抗生素會延長帶菌狀態
  - 臨床恢復後，糞便培養物保持陽性數周

        - 低感染性，需要高度的微生物負荷才能感染
    - 高危人群：兒科和老年患者；愛滋病患者
    - 處裡寵物、煮熟的雞蛋和雞肉，以及污染的炊具
    - 疫苗不是館犯有效的並且通常不被使用

重點

```
- Flegalla(+)
- glicose(+)
- oxidase(-)
- H<sub>2</sub>S
```

耶爾森氏菌屬(Yersinia)

特點

- 人畜共患並，人類是意外宿主
- 皆抗吞噬細胞的毒殺作用，好侵犯淋巴組織
- 嗜鐵菌(Siderophilic bacteria)

主要的致病菌

- *Y.pestis*:引起鼠疫(plague)，不治療有高死亡率。
  - 無鞭毛，雙級染色安全別針樣
  - 毒力為蛋白質*莢膜*(Fra 1)和Pla蛋白酶(質體)
  - 腺鼠疫(buboes)和敗血症鼠疫鼠蚤為媒介
  - 肺鼠疫可經呼吸道傳染
- 其他Yersinia引起機會性疾病

治療

- 鏈黴素為鼠疫感染首選；四環素，氯黴素或甲氧苄氨嘧啶-磺胺甲噁唑可做為替代療法給藥。
- 其他Yersinia的腸道感染通常氏自我限制的
  - 如果需要抗生素治療，大多數生物對廣譜頭孢菌素，氨基糖苷類，氯黴素，四環素類和甲氧苄氨嘧啶-磺胺甲噁唑敏感

預防

- 鼠疫是由控制病媒及病原來管控
  - 減少齧齒動物的人口合疫苗接踵危險人群，疫苗保護期短效果有爭議。
- 其他Yersinia感染通過適當的食品製備來控制

重點

- Flegalla(+)
- glicose(+)
- oxidase(-)

變形桿菌(Proteus)

- 主要引起疾病：泌尿道感染、傷口感染及菌血症
- 菌體運動性強，在寫意培養基上菌落呈遊走傾向，具有獨特的燒焦巧克里味。
- 快速分解 urease
    - 常導致泌尿道感染，分解尿素產生鹼性產物->導致尿道結石
- Proteus的O抗原與立克次體有交叉反應->Weil-Felix試驗

重點

很強的遊走傾向