# Multi-Query Sequence Analysis From CDRs to Constructs 

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## I have a LOT of sequences to search

....and I need combinations and variations! HELP!

Or
I have a due diligence search to perform over the IP portfolio of a company we're considering acquiring, and they have hundreds of sequences....

Or
I need to do a quick screen on early-stage research candidate sequences-a lot of them! Or...I want my researchers to do the initial screen.

Or
I need to share my results with colleagues so they can also view and analyze my searches

## So what can GenomeQuest do for me?

- Search \& analyze as many as 250 sequences simultaneously
- Apply saved (or newly-created) filters \& views and create workflows that can be applied by non-expert users
- Flexible filters, grouping and views allow interaction with specific sequence(s)
- For the more detailed analysis or special projects, create a library of saved analysis parameters, methods and views.
- Create reports or extract sequences in multiple formats
- Standard report formats (Word, Excel, Bizint) facilitate information exchange
- Live result sharing and saved view formats enable real-time collaboration
- Export sequences in standard interchange formats for use in your choice of sequence analysis software (FASTA, EMBL, Genbank)


# Patent Documents with Different Query Combinations 

## VENN DIAGRAM

This is a Venn diagram of your 3 queries with hits to patents. The clickable numbers are the number of patents 1 , 2 or 3 queries hit.


This Venn is available on the "intermediate page" when you search two or three query sequences. By clicking on the numbers on each intersection, you can filter for PNs containing the specified combination of hits.

## Group by Query

For each query sequence, immediately see the hit count and best hit.


## Or in GQ Discover...

- Query Sequence ID
$\square$ repOrigin $(5,475)$
$\square$ oriT $(5,051)$
$\square$ regulatory1 $(16,342)$
$\square$ regulatory2 $(1,387)$
$\square$ lacZ $(100,000)$
$\square$ parE (52)
$\square$ parD (86)
$\square$ parC (27)
$\square$ parB (25)
$\square$ parA (25)
$\square$ aph $(16,342)$
$\square \operatorname{trf}(4,320)$
$\square$ kanamycin_PPT $(24,995)$
- Track the hit count for each query sequence
- Very visible if a query sequence is filtered out
- Query Sequence ID
$\square$ HC-Ebola $(74,100)$LC-Ebola $(914,028)$HCDR1 $(961,786)$HCDR2 $(25,540)$
$\square$ HCDR3 (21)
$\square$ LCDR1 $(464,801)$LCDR2 $(1,000,000)$LCDR3 $(444,158)$


## Grouping

## © GenomeQuest

$\square$ Home > StephanieCA2868330 $(\mathrm{vm})($ vs both $G P)(v m)(v m)($ redo 1$)(v m)>$ Full


Grouped by Patent family ID

| $\star$ | Query <br> Identifier | Identifier | Patent Family ID | Patent Number | Query \% Id | Subj. \% Id |
| :---: | :---: | :---: | :---: | :---: | :---: | :---: |
| $\square$ US10517941 1-1 of 24 [ View all 24 Results ] |  |  |  |  |  |  |
| $\square$ | $\begin{aligned} & \text { CA2868330- } \\ & 0002 \end{aligned}$ | $\begin{aligned} & \text { US10517941- } \\ & 0047 \end{aligned}$ | US10517941 | US10517941 | 94.70 | 94.87 |

```
JS20200040065 100.00 14.84 100.00
```


## And combine grouping with filtering



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# Random Tip Select Families with Grouping \& Date Filters 

```
Group by Patent family ID }>\mathrm{ and show 3 - results per group. New families since 1/1/20
Show only groups with
|ate of entry 
```

Group by Patent family ID $\sim$ and show 1 - result per group. Families with new member(s) since $1 / 2 / 20$
Show only groups with

| Date of entry | $\stackrel{\rightharpoonup}{*}$ | earliest date is before | $\stackrel{\rightharpoonup}{*}$ | 2020 * | January | $\uparrow$ | 1 | - | - | + |
| :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: |
| Date of entry | $\uparrow$ | latest date is later than | $\stackrel{\rightharpoonup}{*}$ | 2020 - | January | $\stackrel{\rightharpoonup}{*}$ | 2 | - | - | + |

## Patent Statistics Report PN Level

- Home > 6_CDR_GP_80 > Full aln results of work

| Result View | Export | Applications |
| :--- | :--- | :--- |
| Filtering $\quad$ EMBOSS | Gi <br> Extract <br> Geneious |  |

Numeric: * - Grouped by Sub, Patent Statistics
Filter Applied $\quad$ Launch New Search


> Also helpful as a way to regenerate the Venn if you started with $>3$ query sequences and then narrowed.

29 documents match 6 of the 6 queries

| PATENT NUMBER | NB QUERIES | QUERY 1 | QUERY 2 | QUERY 3 | QUERY 4 | QUERY 5 | QUERY 6 | PATTERN |
| :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: |
| CA2754113 | 6 | 37-CDR1 | 37-CDR2 | 37-CDR3 | 9-CDR1 | 9-CDR2 | 9-CDR3 | Prrrr |
| CA2851737 | 6 | 37-CDR1 | 37-CDR2 | 37-CDR3 | 9-CDR1 | 9-CDR2 | 9-CDR3 | YYYYY |
| CA2856866 | 6 | 37-CDR1 | 37-CDR2 | 37-CDR3 | 9-CDR1 | 9-CDR2 | 9-CDR3 | YYYYY |
| EP2408816 | 6 | 37-CDR1 | 37-CDR2 | 37-CDR3 | 9-CDR1 | 9-CDR2 | 9-CDR3 | YrYYY |
| JP2012520679 | 6 | 37-CDR1 | 37-CDR2 | 37-CDR3 | 9-CDR1 | 9-CDR2 | 9-CDR3 | PrYYYY |
| JP2014140372 | 6 | 37-CDR1 | 37-CDR2 | 37-CDR3 | 9-CDR1 | 9-CDR2 | 9-CDR3 | YYYYY |
| JP2015214563 | 6 | 37-CDR1 | 37-CDR2 | 37-CDR3 | 9-CDR1 | 9-CDR2 | 9-CDR3 | YYYYYY |
| PP2015505822 | 6 | 37-CDR1 | 37-CDR2 | $37-$ CDR3 | 9-CDR1 | 9-CDR2 | 9-CDR3 | PrYYY |
| JP5498566 | 6 | 37-CDR1 | 37-CDR2 | 37-CDR3 | 9-CDR1 | 9-CDR2 | 9-CDR3 | YYYYY |
| JP5980384 | 6 | 37-CDR1 | 37-CDR2 | 37-CDR3 | 9-CDR1 | 9-CDR2 | 9-CDR3 | YYYYYY |
| JP6203740 | 6 | 37-CDR1 | 37-CDR2 | 37-CDR3 | 9-CDR1 | 9-CDR2 | 9-CDR3 | Prrry |
| KR1020110128948 | 6 | 37-CDR1 | 37-CDR2 | 37-CDR3 | 9-CDR1 | 9-CDR2 | 9-CDR3 | YYYYYY |
| KR1020130067314 | 6 | 37-CDR1 | 37-CDR2 | 37-CDR3 | 9-CDR1 | 9-CDR2 | 9-CDR3 | YYYYY |
| KR20130067314 |  | CDR1 | 37-CDR2 | 37-CDR3 | 9-CDR1 | 9-CDR2 | 9-CDR3 | YYYYYY |
| US20100254975 | xcel export | CDR1 | 37-CDR2 | 37-CDR3 | 9-CDR1 | 9-CDR2 | 9-CDR3 | YYYYY |
| US20120177662 | Excel export | CDR1 | 37-CDR2 | $37-$ CDR3 | 9-CDR1 | 9-CDR2 | 9-CDR3 | YYYYY |
| US20120183561 |  | CDR1 | 37-CDR2 | 37-CDR3 | 9-CDR1 | 9-CDR2 | 9-CDR3 | YYYYY |
| US20130302354 | 6 | 37-CDR1 | 37-CDR2 | 37-CDR3 | 9-CDR1 | 9-CDR2 | 9-CDR3 | Prrry |
| US20140322209 | 6 | 37-CDR1 | 37-CDR2 | $37-$ CDR3 | 9-CDR1 | 9-CDR2 | 9-CDR3 | YYYYY |
| US20150086563 | 6 | 37-CDR1 | 37-CDR2 | 37-CDR3 | 9-CDR1 | 9-CDR2 | 9-CDR3 | YYYYY |
| US20170275365 | 6 | 37-CDR1 | 37-CDR2 | $37-$ CDR3 | 9-CDR1 | 9-CDR2 | 9-CDR3 | MrMY |
| US8444981 | 6 | 37-CDR1 | 37-CDR2 | 37-CDR3 | 9-CDR1 | 9-CDR2 | 9-CDR3 | PYYYY |
| US8454961 | 6 | 37-CDR1 | 37-CDR2 | $37-$ CDR3 | 9-CDR1 | $9-C D R 2$ | 9-CDR3 | YYYYY |
| US8454962 | 6 | 37-CDR1 | 37-CDR2 | 37-CDR3 | 9-CDR1 | 9-CDR2 | 9-CDR3 | YYYYY |
| US8871490 | 6 | 37-CDR1 | 37-CDR2 | 37-CDR3 | 9-CDR1 | 9-CDR2 | 9-CDR3 | PrYYY |
| US9499620 | 6 | 37-CDR1 | 37-CDR2 | 37-CDR3 | 9-CDR1 | 9-CDR2 | 9-CDR3 | PYYYY |
| W02010107752 | 6 | 37-CDR1 | 37-CDR2 | 37-CDR3 | 9-CDR1 | 9-CDR2 | 9-CDR3 | YYYYYY |
| W02013078375 | 6 | 37-CDR1 | 37-CDR2 | 37-CDR3 | 9-CDR1 | 9-CDR2 | 9-CDR3 | Prrry |
| W02017180587 | 6 | 37-CDR1 | 37-CDR2 | 37-CDR3 | 9-CDR1 | 9-CDR2 | 9-CDR3 | YYYYY |

Global Statistics
There were original queries of which 3 have hits
There is a total of 477 patent documents from 204 INPADOC patent families. The earliest priority date is : IN249086 20050202
Venn Diagram of the number of document by matching queries


## Workshop Searches Here

GGenomeQuest


May also have been run in your student account.

## Quick Start

## Launch IP Search

Run IP sequence searches with a simf launch page.

## Practice: Grouping \& Patent Statistics

## Basic: PIUG Practice Ebola LC CDRs 10k (vm)

1. Enter search results by clicking on search name
2. Use Venn to pre-select for PNs comprising all three CDRs
3. Use grouping \& filtering to narrow to chains comprising all three CDRs


## Advanced: PIUG Practice Ebola 6 CDR short name (vm)

1. Go directly to search results
2. Create your own grouping filter to narrow to chains comprising all 3 HC CDRs, then chains comprising all 3 LC CDRs.
3. Experiment with Patent Statistics to find PNs with all 6 CDRs


If you like, try out the new family/new members grouping method as well.

# How about filtering for coordinates? 

Find CDR hits to my chain that cover specific coordinates
f 1 and f 2 and ( $(\mathrm{f} 3$ and f 4 ) or ( f 5 and f6) or ( f 7 and f8))
Gaps removed separately


# Multiple Query Sequence Analysis Working with Chains \& CDRs 

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## Methods - Query Sequence is Chain

To narrow results to just CDRs or just chains, add a subject length (or \% subject coverage) filter. Use query coordinate filters to select for subsequence alignments (e.g. CDR2 only)

Match to only chains
Show results that meet all conditions $\uparrow$


Match to only CDRs
Show results that meet all conditions $\boldsymbol{v}$


The key is the length field
This means "length of hit sequence"

## Practice - Query Sequence is Chain

## PIUG Practice HC full chain (vm)

Click REDO on this search twice; the first time set it as $80 \%$ ID over query; the second time, set it as $80 \%$ ID over query or subject. Set a maximum of 10 k hits both times. How many results do you get for each set of parameters?

| $\square$ | Name | Type |  |
| :---: | :---: | :---: | :---: |
| $\square$ | 等 PIUG ebola HC chain practice [Full aln results] | IP | Redo |



Additional Strategy Parameters
Limit subject length from 6

## Let's get some CDR searches going

## Click REDO for the following searches:

$\square$ 解 PIUG Practice Ebola HC CDR 10 k (vm)
$\square$ PIUG Practice Ebola LC CDRs 10 k (vm)

You are welcome to change the parameters, or just leave them alone for now. We'll use them later.

## Visualizing CDRs



| $\square$ | HCDR3 | EP3525813-0001 | 61905948 | EP3525813 |  |
| :---: | :---: | :---: | :---: | :---: | :---: |
| Alignment | Patent | Subject Annotation | Subject Sequence | Query Sequence | Report data issue |

1. Venn: Detect PNs comprising all three CDRs; any combination of Chain/CDR hits


CDR Searching Review GQ Classic Methods

## 3. Select for CDR:CDR hits only

## Show results that meet all conditions $\uparrow$

2. Select for CDRs hitting chain only

Show results that meet all conditions $\hat{\rightharpoonup}$


Arbitrary
Can also use subject length

Can potentially be a bit lower, depending on CDR length


## Search 3 CDRs, select for chains as a result PNs comprising all 3 CDRs

Show results that meet all conditions $\boldsymbol{\sim}$
Increase subj \% align coverage to $>=\sim 90 \%$ to select
Subj. \% align. cov. $\boldsymbol{*}$ less than $\hat{0}$ for CDR hits instead. For this method, group by PN to find hits in each PN, or use Venn.
Help on this page

Home > CIPO Generic 3 CDR search (vm) > Full aln results of workflow CIPO Generic 3 CDR search (vm)
Result View Export Applications

| Filtering - | Grouping - | $\downarrow_{\mathrm{Z}}^{\mathrm{A}}$ Sorting ${ }^{\text {- }}$ | (c) Sharing - | P Family Portrait | P Family Portrait (Java) | Export PN List |
| :---: | :---: | :---: | :---: | :---: | :---: | :---: |

LifeQuest (a) Browse with ©Q Discover
© Browse with $\subset Q$ Discover (Java)

## tandardView: * - Grouped by Patent number

 =ilter AppliedQuery \% Id
Subj. \% Id
Subj. Start Pos.
Subj. Stop Pos.

| $\square$ | CA3012294-0007 | CDR1 | 118 |
| :---: | :---: | :---: | :---: |
| $\square$ | CA3012294-0007 | CDR2 | 118 |
| $\square$ | CA3012294-0007 | CDR3 | 118 |
| $\square$ | CA3012294-0009 | CDR1 | 448 |
| $\square$ | CA3012294-0009 | CDR2 | 448 |
| $\square$ | CA3012294-0009 | CDR3 | 448 |
| $\square$ | CA3012294-0027 | CDR1 | 118 |
| $\square$ | CA3012294-0027 | CDR2 | 118 |
| $\square$ | CA3012294-0027 | CDR3 | 118 |
| $\square$ | CA3012294-0029 | Query $=$ CDR1, 2 and 3 | 448 |
| $\square$ | CA3012294-0029 |  | 448 |
| $\square$ | ${ }^{\text {cas }}$ For same PN hits, group by PN, aroup contains all |  |  |
| $\square$ | САЗО1<294-טu® |  | 118 | CA3U1L294-008 CA3012294-0087 CA3012294-0089 CA3012294-0089 CA3012294-0089


| CDR2 |
| :---: |
| CDR3 |
| CDR1 |
| CDR2 |
| CDR3 |


| 118 |
| :--- |
| 118 |
| 448 |
| 448 |
| 448 |


| 100.00 | 4.24 | 31 | 35 |
| :---: | :---: | :---: | :---: |
| 100.00 | 14.41 | 50 | 66 |
| 100.00 | 7.63 | 99 | 107 |
| 100.00 | 1.12 | 31 | 35 |
| 100.00 | 3.79 | 50 | 66 |
| 100.00 | 2.01 | 99 | 107 |
| 100.00 | 4.24 | 31 | 35 |
| 100.00 | 14.41 | 50 | 66 |
| 100.00 | 7.63 | 99 | 107 |
| 100.00 | 1.12 | 31 | 35 |
| 100.00 | Variant chain? | 50 | 66 |
| 100.00 |  | 99 | 107 |
| 100.00 | 4.24 | 31 | 35 |
| 94.12 | 13.56 | 50 | 66 |
| 100.00 | Q: | 1 WIDPGQSNTRYSPSFQG 17 <br> 50 WIDPGTSNTRYSPSFOG <br> 66 | 107 |
| 100.00 |  |  | 35 |
| 94.12 |  |  | 66 |
| 100.00 |  |  | 107 |

# Search for <br> PNs comprising all 6 Query CDRs 

## Q GenomeQuest

- Home > Ebola 6 CDR short name > Full aln results of workflow Ebola 6 CDR short name

<< First < Previous Patent number 1-4 of 4 Next > Last >>



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## Searching for chains comprising all three CDRs

## Method 1: MOTIF on Full Length Chain Direct Strike



This is the method Danie Kolker from the USPTO talked about yesterday - concatenating all three CDRs.

The long sequence gives hits comprising all three CDRs in the specific order provided, with 100\% identity to each CDR (or variations as specified). Represents "any number of unspecified residues, including zero".

```
>37-motif
DLSIH.*GFDPQDGETIYAQKFQG.*GSSSSWFDP
>9-motif
RA[ST]QGISSWLA.*GASNLES.*QQANSFPWT
```


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## Method 2: Group \& Filter, GQ Classic (Review)



Select for subjects comprising all three CDRs (or a subset of CDRs) or for CDR:CDR matches instead (or sequentially).


| Show results that |  | all conditions |  |  |
| :---: | :---: | :---: | :---: | :---: |
|  | CDR:CDR matches |  |  |  |
| Subj. \% align. cov. | $\uparrow$ | equals | $\stackrel{\rightharpoonup}{*}$ | 100 |

## Method 3: 3 click analysis in GQ Discover



## What are＂Unique Sequences＂？

```
Simple Unique Family Sequence ID 61905948－5
－Patent Family 61905948
```

| $\square{ }^{\text {ath }}$ | －HCDR1 |
| :---: | :---: |
| $\square{ }^{\text {a }}$ | －HCDR2 |
| $\square$ 介介穴 | －HCDR3 |
| $\square{ }^{\text {a }}$ | －HCDR1 |
| $\square{ }^{\circ}+$ | －HCDR2 |
| $\square \wedge$ ¢ | －HCDR3 |
| $\square)^{\text {a }}$ | －HCDR1 |
| $\square{ }^{-1}$ | －HCDR2 |
|  | －HCD |

WO2018071345－0001
WO2018071345－0001
WO2018071345－0001
EP3525813－0001
EP3525813－0001
EP3525813－0001
CN110087677－0001
CN110087677－0001
CN110087677－0001

Query 100．0\％
Query 100．0\％
Query 100．0\％
Query 100．0\％
Query 100．0\％
Query 100．0\％
Query 100．0\％
Query 100．0\％
Query 100．0\％
－This is the UFS we use regularly
－It is the identical sequence， segregated by patent family． regated by patent family．
－Simple Unique Family Sequence ID US20200040065－5
－Patent Family US20200040065


US20200040065－0001
US20200040065－0001
US20200040065－0001

Query 100．0\％
Query 100．0\％
Query 100．0\％

SEQ ID NO 1
SEQ ID NO 1
SEQ ID NO 1

SEQ ID NO 1
SEQ ID NO 1
SEQ ID NO 1
SEQ ID NO 1
SEQ ID NO 1
SEQ ID NO 1
SEQ ID NO 1
SEQ ID NO 1
SEQ ID NO 1

# Q GenomeQuest Our upcoming release.... 

## One click finds the needle in >1 million result haystack....

## My Column Groups

$\boxplus$ Select Displayed Columns -Saved Views

Highlight Text
Highlight all text

Filter Text

- Query Sequence ID

HCDR1 $(300,000)$
HCDR2 $(25,529)$
$\square$ HCDR3 (21)
LCDR1 $(300,000)$
$\square$ LCDR2 $(300,000)$
$\square$ LCDR3 $(300,000)$
Patent Numbers

- Sequence Databases
- Annotation Filters
- Patent Authorities
- Extended Legal Status
- Patent Sequence Location
- Advanced Filters

GQ Power Tools

- Sequence Variation Discovery (i)
- Variation Filters
$\boxplus$ Create New Variation Filter
- Global Filters
- Result-specific Filters

Variation Landscape


Multiple Query Sequence Analysis

## From 1.2 million to 64 results

## G GenomeQuest

| My Column Groups |
| :--- |
| Đ Select Displayed Columns |
| - Saved Views |
| Highlight Text |
| Highlight all text |
| Filter Text |
| Search all text |
| - Query Sequence ID |
| $\square$ HCDR1 (8) |
| $\square$ HCDR2 (12) |
| $\square$ HCDR3 (8) |
| $\square$ LCDR1 (12) |
| $\square$ LCDR2 (8) |
| $\square$ LCDR3 (16) |
| - Patent Numbers |
| - Sequence Databases |
| Annotation Filters |
| - Patent Authorities |
| Extended Legal Status |

## 3 CDR Report Creation GQ Classic

## © GenomeQuest



You could even make group size $=1$, then export top 1 result/subject, given that each subject comprises the three CDRs

## Practice Finding CDRs

Use either PIUG practice Ebola HC CDR 10k search or LC CDR 10k search you started earlier

1. Use the Venn diagram as an entry point to your results. Note how many PNs contain all three CDRs
2. Move to GQ Discover. Does the MQSA show the same PN count?
3. Click on your choice of PNs or Unique Sequences containing all 3 query sequences.
4. Group by patent family, sort by Subject Sequence ID for a clear view. You may want to make some column selections to better understand your data.


## Multiple Query Sequence Analysis

matching all 3 query seqs: • 2 Patent Families

- 4 Patent Numbers
- 2 Unique Sequences
matching 2 out of 3 query seqs:
matching 1 out of 3 query seqs:

Total
matching at least one query seq

- 2 Patent Families
- 4 Patent Numbers
- 2 Unique Sequences

Part 2 - going back
Check your result count on PIUG Practice HC full chain (vm) for the two different methods (we did this REDO earlier). What did you see?

## Moving on to some claims

## HC Analysis

wherein the VH comprises heavy chain complementarity determining regions CDRH1, CDRH2, and CDRH3, wherein CDRH1 comprises SEQ ID NO: 3 or SEQ ID NO: 3 with one or two single amino acid substitutions, wherein the substitutions are at positions XI and/or X2 of G-Y-Y-X1-W-X2 (SEQ ID NO: 9); wherein CDRH2 comprises SEQ ID NO: 4, or SEQ ID NO: 4 with one, two, or three single amino acid substitutions; and wherein CDRH3 comprises SEQ ID NO: 5 or SEQ ID NO: 5 with one, two, or three single amino acid substitutions, wherein the substitutions are at positions XI, X2, X3, X4, X5, X6, X7, X8, X9, X10, XI 1, and/or X12 of D-X1-G-X2-T-I-F-X3-X4-X5-I-X6-X7-W-X8-X9-X10-D-X12 (SEQ ID NO: 10); and

How painful is it to interpret and write the query for SID 9 or $10 ?$ Let's start off simple..

## Custom Boolean Replacement Count and Query Identifier

| (f1 and f2) or ((f3 or f4) and f5) $\begin{aligned} & \text { HC-CDR1: up to } 2 \text { replacements } \\ & \\ & \text { HC-CDR2 \& 3: up to } 3 \text { replaceme }\end{aligned}$ |  |  |  |  |  |  |  |
| :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: |
| F1 | Query Sequence ID | $\checkmark$ | contains | $\checkmark$ | HCDR1* | - | + |
| F2 | Diff. Count | $\checkmark$ | less than or equal | $\checkmark$ | 2 | - | + |
| F3 | Query Sequence ID | $\checkmark$ | contains | $\checkmark$ | hcdr2* | - | + |
| F4 | Query Sequence ID | $\checkmark$ | contains | $\checkmark$ | hcdr3* | - | + |
| F5 | Diff. Count | $\checkmark$ | less than or equal | $\checkmark$ | 3 | - | + |

## Comprising all three

We dodged a bullet！

－US20200040065

|  | －HCDR1－WO2018071345－0003 |
| :---: | :---: |
|  | －HCDR2－WO2018071345－0004 |
|  | －HCDR3－WO2018071345－0005 |

－EP3525813


－HCDR3－WO2018071345－0005
－CN110087677

- $\square$ 加軲 $\square$ HCDR1－WO2018071345－0003
- $\square$ 制朝 $\square$ HCDR2－WO2018071345－0004
$— \square$ ）$\quad$－HCDR3－WO2018071345－0005
－WO2018071345

- $\square$ 軲 $\square$ • HCDR2－WO2018071345－0004
- $\square$ 軲 $\square$ • HCDR3－WO2018071345－0005

|  |  |
| :---: | :---: |
| Query 100．0\％ | US20200040065－0001 |
| Query 100．0\％ | US20200040065－0001 |
| Query 100．0\％ | US20200040065－0001 |
| Query 100．0\％ | EP3525813－0001 |
| Query 100．0\％ | EP3525813－0001 |
| Query 100．0\％ | EP3525813－0001 |
| Query 100．0\％ | CN110087677－0001 |
| Query 100．0\％ | CN110087677－0001 |
| Query 100．0\％ | CN110087677－0001 |
| Query 100．0\％ | WO2018071345－0001 |
| Query 100．0\％ | WO2018071345－0001 |
| Query 100．0\％ | wo2018071345－0001 |

## If mismatches were found, however....

wherein the VH comprises heavy chain complementarity determining regions CDRH1, CDRH2, and CDRH3, wherein CDRH1 comprises SEQ ID NO: 3 or SEQ ID NO: 3 with one or two single amino acid substitutions, wherein the substitutions are at positions XI and/or X2 of G-Y-Y-X1-W-X2 (SEQ ID NO: 9); wherein CDRH2 comprises SEQ ID NO: 4, or SEQ ID NO: 4 with one, two, or three single amino acid substitutions; and wherein CDRH3 comprises SEQ ID NO: 5 r SEQ ID NO: 5 with one, two, or three single amino acid substitutions, wherein the substitutions are at positions XI, X2, X3, X4, X5, X6, X7, X8, X9, X10, XI 1, and/or X12 of D-X1-G-X2-T-I-F-X3-X4-X5-I-X6-X7-W-X8-X9-X10-D-X12 (SEQ ID NO: 10); and
8. The antibody or fragment thereof of claim 6 or claim 7 , wherein any one amino acid at position XI, X2, X3, X4, X5, X6, X7, X8, X9, X10, XI 1, or X12 of SEQ ID NO: 10 is substituted with alanine, any two amino acids at positions XI, X2, X3, X4, X5, X6, X7, X8, X9, X10, XI 1, or X12 of SEQ ID NO: 10 are substituted with alanine, or any three amino acids at positions XI, X2, X3, X4, X5, X6, X7, X8, X9, X10, XI 1 , or X12 of SEQ ID NO: 10 are substituted with alanine.

Even though there are some very specific variation claims, because we filtered by number of differences and found nothing >0 differences, we don't have to go any further.

Had there been any hits with variations, GQ's Sequence Variation Discovery Module would have enabled quick determination of the presence of the recited substitutions...which would have been very simple because only alanine is stated.

We'll use light chain as an example to illustrate this method

## W02018071345 <br> LC Claim Section, Claim 6

wherein the VL comprises light chain complementarity determining regions CDRL1, CDRL2, and CDRL3, wherein CDRL1 comprises SEQ ID NO: 6, or SEQ ID NO: 6 with one, two, or three single amino acid substitutions; wherein CDRL2 comprises SEQ ID NO: 7, or SEQ ID NO: 7 with one, two, or three single amino acid substitutions; and wherein CDRL3 comprises SEQ ID NO: 8, or SEQ ID NO: 8 with one, two, or three single amino acid substitutions.

Translation: filter for CDRL1-3 with number of differences <=3

Show results that $\quad$ meet all conditions $\quad$ First the regular search....

| No. diff $\stackrel{\rightharpoonup}{\text { a }}$ | less than or equal to $\stackrel{\rightharpoonup}{\text { a }}$ | 3 |
| :---: | :---: | :---: |
| Subj. number of gaps $\boldsymbol{\wedge}$ | equals $\quad \stackrel{\rightharpoonup}{\text { v }}$ | 0 |
| Query number of gaps $\boldsymbol{\wedge}$ | equals $\quad \stackrel{\rightharpoonup}{\text { v }}$ | 0 |

## GQ Discover <br> How to Identify Variations



| Multiple Query Sequence Analysis |  |
| :---: | :---: |
| matching all 3 query seqs: | - 3 Patent Families <br> - 11 Patent Numbers <br> - 4 Unique Sequences |
| matching 2 out of 3 query seqs: matching 1 out of 3 query seqs: |  |
| Total <br> matching at least one query seq | - 3 Patent Families <br> - 11 Patent Numbers <br> - 4 Unique Sequences |

- Use MQSA to find chains comprising all three CDRs, then export a variation landscape.
- Prefilter as appropriate (diffs, query ID, etc)

GQ Power Tools

- Sequence Variation Discovery ${ }^{(1)}$
- Variation Filters
- Variation Landscape
- LCDR1-WO2018071345-0006 (3

5) 

create

- LCDR2-WO2018071345-0007 (3

0) 

create

- LCDR3-WO2018071345-0008 (3

5) 

create

# Variation Landscape Overview Narrow Resultset 

RASQSISNNL A
LC-CDR1

| Query <br> position | Variation type | Description |
| :---: | :--- | :--- |
| 11 | Replacement | A 11 N (14) |

AASNLA
LC-CDR2

| Query position | Variation type | Description |
| :--- | :--- | :--- |

No variations found

QQHNTLPLT
LC-CDR3

| Query <br> position | Variation type | Description |
| :--- | :--- | :--- |
| 3 | Replacement | H3S (14) |
| 6 | Replacement | L6S (14) |

This output shows variations in individual CDR positions when all three are present on a single chain.

- This was created by using MQSA to identify chains comprising all three CDRs.
- Remove the requirement for all 3 CDRs to be present to study CDR variations in isolation
- Use filters to limit to just CDR:CDR matches if preferred.
- Create virtual database of CDR results and search chain against that for chain variations in CDR regions.

The above output is from three separate Variation Landscape Reports, available with GQ's Sequence Variation Discovery Module

Let's take it further - Let's create a landscape for our three CDR regions.
Use chain as query here

## A aptean

## Create vDB from CDR Search Hits



Create virtual database of CDR results and search chain against that for chain variations in CDR regions.

Why vDB? Just to have a narrow resultset to search chain against

If you want to follow along, the database already exists in our shared data folder.


## Normal GQ Search vs vDB



Additional Strategy Parameters
Limit subject length from 6 to 1000 residues
Keep a maximum of 250000 results (per query)

Use GQ view to identify CDR positions for next step

| Identifier | Query Start Pos. | Query Stop Pos. |
| :---: | :---: | :---: |
| WO2018071345-0006 | 24 | 34 |
| WO2018071345-0008 | 89 | 97 |
| WO2018071345-0007 | 50 | 55 |

Subject Databases ${ }^{2}$

- Apply filters to subject databases

```
Nucleotides
+| Patents
# | Reference Data
D Data Shared With Me
\square My Data
```

Proteins
$\square$ Reference Data

- My Data
$\pm \square$ BGN
ebola CDR nogap vdb
] ebolaWTvdb
piug ebola comprise all 3

| PIUG Biotech |
| :--- |
| PIUG LC 3 cdr db |

PIUG LC 3 cdr db
PIUG WO2018071345 HC full chain only
PIUG WO2018071345 LC full chain
vDB shows up in My Data or Data Shared with Me

# GQ Discover: <br> Filter to Create Tightly-Targeted Variation Report 

Results must meet all conditions at least one condition
PIUG CDRs align to chain \& ce
f 1 and f 2 and ( $(\mathrm{f} 3$ and f 4 ) or (f5 and f6) or ( f 7 and f8))
Optionally limit to hits covering CDR coordinates

| F1 | Subject Sequence Le | $\checkmark$ | less than or equal | $\checkmark$ | 25 | - | + | Create landscape |
| :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: |
| F2 | Diff. Count | $\checkmark$ | less than or equal | $\checkmark$ | 3 | - | + |  |
| F3 | Query Start Position | $\checkmark$ | less than or equal | $\checkmark$ | 24 | - | + |  |
| F4 | Query Stop Position | $\checkmark$ | more than or equal | $\checkmark$ | 34 | - | + |  |
| F5 | Query Start Position | $\checkmark$ | less than or equal | $\checkmark$ | 50 | - | $+$ |  |
| F6 | Query Stop Position | $\checkmark$ | more than or equal | $\checkmark$ | 55 | - | + |  |
| F7 | Query Start Position | $\checkmark$ | less than or equal | $\checkmark$ | 89 | - | $\pm$ |  |
| F8 | Query Stop Position | $\checkmark$ | more than or equal | $\checkmark$ | 97 | - | + |  |

## Create \& Export Variation Landscape

- rIUG <=0 ullı LU
- PIUG CDRs align to chain \& co
$\square$ PIUG complex HC CDRPIUG Ebola chain queryPIUG Ebola LC querysubtilase cas family dedupeWO2010056640-subtl demo


## GQ Power Tools

- Sequence Variation Discovery ${ }^{1}$
- Variation Filters
$\boxplus$ Create New Variation Filter
- Global Filters
- Result-specific Filters
- Variation Landscape
- LC-Ebola $(43,052)$ create

Variation Landscape Summary Table

| Query position | Variation type | Description |
| :---: | :---: | :---: |
| 24 | Replacement | R24K(11), R24Q(354) |
| 25 | Replacement | A25ㄹ(4), A25T(2) |
| 26 | Replacement | S26N(16), S26Q(9) |
| 27 | Replacement | Q27E(31), Q27H(5), Q27K(3), Q27P(10), Q27R(11) |
| 28 | Replacement | S28AP76), S28D(517), S28G(2841), S28N(17), S28P(6), S28R(15), S28T(62), S28V(44), S28Y(14) |
| 29 | Replacement | 129L(19), L29M(27), $129 \mathrm{~S}(16)$, $129 \mathrm{~V}(2707$ ), $129 \mathrm{~W}(1), \mathrm{I29X}(10)$ |
| 30 | Replacement | S30A(32), S30F(43), S30G(186), S30H(4), S301(24), S30K(64), S30L(6), S30N(127), S30R(111), S30T(19), S30V(10), S30W(1), S30Y(85) |
| 31 | Replacement | N31A(4), N31D(71), N31E(16), N31F(31), N31G(50), N31H(66), N311(30), N31K(18), N31R(333), N31S(10307), N31T(295), N31V(28), N31Y(79), N31Z( 3) |
| 32 | Replacement | N32A(60), N32C(6), N32D(263), N32F(3959), N32G(2), N32H(150), N321(2), N32L(109), N32Q(92), N32R(79), N32S(340), N32T(14), N32W(5671), N32 $\mathrm{Y}(3378)$ |
| 33 | Replacement | L33V(52) |
| 34 | Replacement | A34G(11), A34H(828), A341(5), A34L(14), A34N(977), A34Q(27), A34S(37), A34T(2), A34V(31), A34X(3) |
| 35 | Replacement | W35I(18), W35Z(16) |
| 39 | DIQMTQSPSS LSASVGDTVT ITCRASQSIS NNLAWYQQRP RRAPQLLIYA ASN ASGVPS RFSGSGSGTD FTLTISSLQA EDFAAYYCQQ HNTLPLTEGG GTKVEI | R39K(17) |
| 46 |  | L46A(1), L46P(111), L46R(1), L46S(1), L46T(1) |
| 47 |  | L47A(1), L47K(4), L47W(119) |
| 48 |  | $148 \mathrm{~A}(4)$, $148 \mathrm{~L}(1)$, $148 \mathrm{~S}(4), 148 \mathrm{~V}(24)$ |
| 49 | Replacement | Y49A(18), Y49D(3), Y49F(2), Y49G(8), Y49H(1), Y491(8), Y49K(1), Y49N(9), Y49P(15), Y49Q(1), Y49S(7), Y49V(4) |
| 50 | Replacement | A50D(186), A50G(483), A50H(3), A50K(78), A50L(68), A50Q(164), A50R(418), A50S(182), A50T(39), A50V(12), A50W(3) |
| 51 | Replacement | A51C(2), A51D(2), A51E(2), A51F(2), A51G(4), A51H(5), A511(26), A51K(3), A51L(2), A51M(2), A51N(2), A51P(367), A51Q(2), A51R(2), A51S(39), A51 $\mathrm{T}(1828), \mathrm{A} 51 \mathrm{~V}(8), \mathrm{A} 51 \mathrm{~W}(2), \mathrm{A} 51 \mathrm{X}(1), \mathrm{A} 51 \mathrm{Y}(2)$ |
| 52 | Replacement | S52A(12), S52F(52), S52I(1), S52K(9), S52M(36), S52R(34), S52T(1046) |
| 53 | Replacement | N53D(30), N53F(43), N53G(3), N531(8), N53K(90), N53L(34), N53P(36), N53R(10), N53S(50), N53T(165), N53Y(9) |
| 54 | Replacement | L54E(3), L54G(3), L541(3), L54N(3), L54Q(5), L54R(98), L54T(6), L54V(7) |
| 55 | Replacement | A55过(132), A55E(8012), A55G(61), A55H(64), A551(21), A55K(101), A55P(6), A55Q(1074), A55R(59), A55S(3), A55T(1), A55X(7), A55Y(37)\| |
| 56 | Repl: | S56A(58). S56C(2). S56D(1358). S56E(17). S56F(141). S56H(2), S56l(17), S56K(19), S56L(5), S56M(2), S56N(25), S56P(26), S56Q(6), S56R(39), S56 |
| 57 | Repl Remember the ALA in HC claims 7 \& 8? We'd look for A in |  |
| 58 | eepli any of the recited positions; if found we'd build appropriate |  |
| 60 |  |  |
| 88 | epli variation filters |  |
| 89 |  |  |
| 91 | Replacement | H91A 141 ), H91F(17), H91G(5713), H91L(66), H91R(9), H91S(181), H91T(82), H91V(4), H91W(4), H91Y(204) |
| 92 | Replacement | N92D(87), N92E(10), N92F(17), N92H(11), N92K(33), N92S(11), N92Y(131) |
| 93 | Replacement |  |
| 94 | Replacement | L94A(6), L94D(73), L94F(64), L94H(3), L941(33), L94N(73), L94P(4), L94S(68), L94T(105), L94W(116), L94Y(551) |
| 96 | Replacement | L96A(8), L96F(98), L96H(8), L961(12), L96P(236), L96R(45), L96W(1174), L96X(3), L96Y(4067) |
| 98 | Replacement | F98I(4) |
| 100 | Replacement | G100S ${ }^{(5)}$ |
| 102 | Replacement | T102C(8) |

# Multiple Query Sequence Analysis Combinations of Components Constructs \& Elements 

## Find Component Combinations Interactively in GenomeQuest

## GQ Classic

## GQ Discover

## GenomeQuest

$\square$ Home > PIUG PMR elements (vm) > Full aln results of workflow PIUG PMR elements (vm)


- PN level combinations via Patent Statistics
- Or use grouping and grouping filters to narrow to subjects comprising multiple specific components


## Q GenomeQuest

My Column Groups $4 \leq \mid \boldsymbol{\sim}$
$\boxplus$ Select Displayed Columns

- Use Query Identifier checkboxes to narrow to specific subject combinations, followed by MQSA for drilldown.
- MQSA single-click identification of subjects or PNs comprising multiple query sequences.

Export from either browser into Excel and use pivot table to get quick \& easy component combination analysis

## GQ Classic 13 Query Sequences



Identify sequences comprising specific query sequence combinations, either at patent number or sequence level

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# GQ Classic <br> Group \& Filter - Direct Strike (What we did with CDR searches) 

Group by Subject $\quad$ and show $1 \rightarrow$ result per group.
Show only groups with

| Query Identifier | $\uparrow$ | one member matches | $\uparrow$ | lacZ | [+] | - | + |
| :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: |
| Query Identifier | $\uparrow$ | one member matches | - | oriT | [+] | - | + |
| Query Identifier | $\uparrow$ | one member matches | - | regulatory1 | [+] | - | + |
| Query Identifier | $\uparrow$ | one member matches | $\checkmark$ | trfA | [+] | - | + |

Works perfectly and is highly specific. Excellent for CDRs

\title{

GQ Classic

# Broader Search (Pivot Setup) 

}

- Home > PIUG PMR elements (vm) > Full aln results of workflow PIUG PMR elements (vm)



Here we are just filtering by group size, not specific query sequences comprised by a subject.

Next step (after filtering for \% identity or any other attributes), is to export as Excel, and then prepare a pivot table.

## GQ Discover <br> Multiple Query Sequence Analysis

Select query sequences to combine, click MQSA button

```
    - Query Sequence ID
    \square \text { repOrigin (2,696)}
    \square \mp@code { o r i T ~ ( 3 , 8 9 6 ) }
    \square \text { regulatory1 (16,089)}
    \square \text { regulatory2 (1,332)}
    \square \mp@code { l a c Z ~ ( 8 8 , 3 1 8 ) }
    \square \text { parE (47)}
    \square \text { parD (77)}
    parC (26)
    \square \text { parB (23)}
parA (0)
    O aph (16,089)
    \square trfA (4,304)
     kanamycin_PPT (18,752)
                            Previously filtered out
```



(1) Co OFF
$\square$ 为加 $\square \rightarrow$ Current Page Unannotated

| Multiple Query Sequence Analysis |  |
| :--- | :--- |
| matching all 6 query seqs: | - 1 Patent Families |
| matching 5 out of 6 query seqs: | - 172 Patent Families |
|  | - 747 Patent Numbers |
| matching 4 out of 6 query seqs: | - 549 Patent Families |
|  | - 2,003 Patent Numbers |
|  | - 1 Unique Sequences |
| matching 3 out of 6 query seqs: | - 1,807 Patent Families |
|  | - 7,583 Patent Numbers |
| matching 2 out of 6 query seqs: | - 3,900 Patent Families |
|  | - 16,765 Patent Numbers |
| matching 1 out of 6 query seqs: | - 2,997 Unique Sequences |
|  | - 56,981 Patent Families |
|  | - 179,582 Unique Sequences |



# Pivot Table Component Analysis Subject Sequence Level Analysis 



## Summary

- GQ gives you the ability to search and analyze resultsets with multiple query sequences
- Drill down to a specific subset, then back up to the full set or a different subset
- Analyze and report on various groupings or all
- Saving views and filters makes life easier for both experienced and inexperienced users
- Variation searches are tedious and painful!
- Use the variation landscape for a high-level overview


## Thank You!

## Questions?

Akua.Akuamoah@aptean.com
Bill.Perkins@aptean.com
Stephen.Allen@aptean.com
Ellen.Sherin@aptean.com


## W02018071345A1

wherein the VH comprises heavy chain complementarity determining regions CDRH1, CDRH2, and CDRH3, wherein CDRH1 comprises SEQ ID NO: 3 or SEQ ID NO: 3 with one or two single amino acid substitutions, wherein the substitutions are at positions XI and/or X2 of G-Y-Y-X1-W-X2 (SEQ ID NO: 9); wherein CDRH2 comprises SEQ ID NO: 4, or SEQ ID NO: 4 with one, two, or three single amino acid substitutions; and wherein CDRH3 comprises SEQ ID NO: 5 or SEQ ID NO: 5 with one, two, or three single amino acid substitutions, wherein the substitutions are at positions XI, X2, X3, X4, X5, X6, X7, X8, X9, X10, XI 1, and/or X12 of D-X1-G-X2-T-I-F-X3-X4-X5-I-X6-X7-W-X8-X9-X10-D-X12 (SEQ ID NO: 10); and
wherein the VL comprises light chain complementarity determining regions CDRL1, CDRL2, and CDRL3, wherein CDRL1 comprises SEQ ID NO: 6, or SEQ ID NO: 6 with one, two, or three single amino acid substitutions; wherein CDRL2 comprises SEQ ID NO: 7, or SEQ ID NO: 7 with one, two, or three single amino acid substitutions; and wherein CDRL3 comprises SEQ ID NO: 8 , or SEQ ID NO: 8 with one, two, or three single amino acid substitutions.
7. The antibody or fragment thereof of claim 6, wherein the amino acid at position XI of SEQ ID NO: 9 is substituted with alanine, the amino acid at position X2 of SEQ ID NO: 9 is substituted with alanine, or the amino acids at positions XI and X2 of SEQ ID NO: 9 are substituted with alanine.

1. Search chains \& CDRs GenePast, $65 \%$ over query
2. Group/MQW for chains comprising all 3 (first filter for subj seq length $>40$ to get chains, q seq length $<40$ to get CDRs.
3. HC first query id contains *HC*- comprises all 3
4. Annotate all 3 red
5. Filter SID3, pos 4 or 6 for ala; annotate 1 star (red and 1 star means has variant SID3. Generate landscape report.

## 6. Red \& 1 star

7. Filter SID 4 broad, mark 2 star

## WO2018071345A1 plan b

wherein the VH comprises heavy chain complementarity determining regions CDRH1, CDRH2, and CDRH3, wherein CDRH1 comprises SEQ ID NO: 3 or SEQ ID NO: 3 with one or two single amino acid substitutions, wherein the substitutions are at positions XI and/or X2 of G-Y-Y-X1-W-X2 (SEQ ID NO: 9); wherein CDRH2 comprises SEQ ID NO: 4, or SEQ ID NO: 4 with one, two, or three single amino acid substitutions; and wherein CDRH3 comprises SEQ ID NO: 5 or SEQ ID NO: 5 with one, two, or three single amino acid substitutions, wherein the substitutions are at positions XI, X2, X3, X4, X5, X6, X7, X8, X9, X10, XI 1, and/or X12 of D-X1-G-X2-T-I-F-X3-X4-X5-I-X6-X7-W-X8-X9-X10-D-X12 (SEQ ID NO: 10); and
wherein the VL comprises light chain complementarity determining regions CDRL1, CDRL2, and CDRL3, wherein CDRL1 comprises SEQ ID NO: 6, or SEQ ID NO: 6 with one, two, or three single amino acid substitutions; wherein CDRL2 comprises SEQ ID NO: 7, or SEQ ID NO: 7 with one, two, or three single amino acid substitutions; and wherein CDRL3 comprises SEQ ID NO: 8 , or SEQ ID NO: 8 with one, two, or three single amino acid substitutions.
7. The antibody or fragment thereof of claim 6, wherein the amino acid at position XI of SEQ ID NO: 9 is substituted with alanine, the amino acid at position X2 of SEQ ID NO: 9 is substituted with alanine, or the amino acids at positions XI and X2 of SEQ ID NO: 9 are substituted with alanine.

1. Search chains \& CDRs GenePast, $65 \%$ over query
2. Group for chains comprising all 3 , make vdb
3. Search against these chains and do vm analysis. Since they already comprise all 3 I don't have to annotate them, so I can do the variants and not out the ones with non-specified mismatches.
4. The goal is less about finding the ones in scope than it is notting out the ones out of scope.
5. I wonder if for sid5 I'd be better off to fix the stated residues, and do a query \% ID cutoff for the rest. 19 residues/3 mismatches $84.2 \%$ QID and just fix pos 1,3,5,6,7,

## Additional CDR Methods

## Results Pre \& Post filtering Patent-Level Grouping



### 1.3K sequences



## Motif - Targeted Results

## G GenomeQuest

| Filtering | ${ }^{\text {G }}$ Grouping - | $\downarrow_{\mathrm{Z}}^{\mathrm{A}}$ Sorting ${ }^{\text {- }}$ | (6) Sharing - | P Family Portrait | Export PN List | $\checkmark$ | 4 LifeQuest | N Try Out New Interface |
| :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: |

1_GP_view: - Grouped by Patent family ID
<< First < Previous Patent family ID 1 -31 of 31 Next > Last >>


Alignment Patent Subject Annotation Subject Sequence Query Sequence Report data issue

- See all subjects mapped to this query
- See all queries mapped to this subject

A part of your query matches a part of this sequence. $G Q$ subject-centric view.
Align len $=82$ aa, ${ }^{\prime}$, Identity $=1008$, similarity $=1008$


Q: $\quad 61$ TavyYcaripgasyypypudy 82


## Method 3 Search within Hits (Use for Huge Resultsets)

1. Search just LC and HC full length
2. Filter for $80 \%$ (or appropriate) query identity, zero gaps, which will only return full length hits and omit CDR and non-specific short hits.
3. Export filtered results to custom database (optionally separate LC from HC; this would result in two custom databases if desired-filter first for query id=LC, extract, then filter for query id=HC, extract)
4. Search all 3 (or 6) corresponding CDRs against appropriate custom db
5. Filter for desired \% ID/\# of differences
6. Use group by subject, filter for query identifier = method shown earlier



## A aptean

# GQ Patent Statistics Grouping on Steroids 

## Table of Contents

Global Statistics
Number of documents per query
Number of documents by authority

## Global Statistics

There were original queries of which 11 have hits
There are 90985 hits to the patent databanks.
There is a total of 16128 patent documents from 4806 INPADOC patent families. The earliest priority date is: EP134242 19830128

## Number of documents per query

Spreadsheet of all hits classified by patents.
2 documents match 7 of the 11 queries

50 documents match 6 of the 11 queries
This is on the patent number level...a little later we will talk about identifying hit sequences comprising different combinations of query sequences

165 documents match 5 of the 11 queries

171 documents match 4 of the 11 queries

1627 documents match 3 of the 11 queries

3104 documents match 2 of the 11 queries

11009 documents match 1 of the 11 aueries


## Patent Statistics Report PN Level

| Result | View | Export | Applications |  |
| :---: | :---: | :---: | :---: | :---: |
| Filtering <br> Gr |  |  | EMBOSS <br> Extract <br> Geneious |  |
|  |  |  |  |  |
| Numeric: * - Grouped by Sub. Filter Applied |  |  | Patent Statistics |  |
|  |  |  | Launch New Search * Bizint Smart Charts Clustalw Vector NTI |  |
| $\because \square$ | Query <br> Identifier Pat |  |  |  |

29 documents match 6 of the 6 queries

| PATENT NUMBER | NB QUERIES | QUERY 1 | QUERY 2 | QUERY 3 | QUERY 4 | QUERY 5 | QUERY 6 | PATTERN |
| :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: |
| CA2754113 | 6 | 37-CDR1 | 37-CDR2 | 37-CDR3 | 9-CDR1 | 9-CDR2 | 9-CDR3 | YrYrr |
| CA2851737 | 6 | 37-CDR1 | 37-CDR2 | $37-\mathrm{CDR} 3$ | 9-CDR1 | 9-CDR2 | 9-CDR3 | YYYYY |
| CA2856866 | 6 | 37-CDR1 | 37-CDR2 | $37-\mathrm{CDR} 3$ | 9-CDR1 | 9-CDR2 | 9-CDR3 | YYYYY |
| EP2408816 | 6 | 37-CDR1 | 37-CDR2 | 37-CDR3 | 9-CDR1 | 9-CDR2 | 9-CDR3 | YYYYY |
| P2012520679 | 6 | 37-CDR1 | 37-CDR2 | $37-\mathrm{CDR} 3$ | 9-CDR1 | $9-C D R 2$ | 9-CDR3 | YYYYY |
| P2014140372 | 6 | 37-CDR1 | 37-CDR2 | 37-CDR3 | 9-CDR1 | 9-CDR2 | 9-CDR3 | YYYYY |
| JP2015214563 | 6 | 37-CDR1 | 37-CDR2 | 37-CDR3 | 9-CDR1 | 9-CDR2 | 9-CDR3 | YYYYY |
| P2015505822 | 6 | 37-CDR1 | 37-CDR2 | $37-\mathrm{CDR3}$ | $9-C D R 1$ | 9-CDR2 | 9-CDR3 | YrYYY |
| JP5498566 | 6 | 37-CDR1 | 37-CDR2 | $37-\mathrm{CDR} 3$ | 9-CDR1 | 9-CDR2 | 9-CDR3 | YYYYYY |
| JP5980384 | 6 | 37-CDR1 | 37-CDR2 | $37-\mathrm{CDR} 3$ | 9-CDR1 | 9-CDR2 | 9-CDR3 | YYYYY |
| JP6203740 | 6 | 37-CDR1 | 37-CDR2 | $37-\mathrm{CDR3}$ | $9-C D R 1$ | 9-CDR2 | 9-CDR3 | YrYYY |
| KR1020110128948 | 6 | 37-CDR1 | 37-CDR2 | $37-\mathrm{CDR} 3$ | 9-CDR1 | 9-CDR2 | 9-CDR3 | YYYYY |
| KR1020130067314 | 6 | 37-CDR1 | 37-CDR2 | 37-CDR3 | 9-CDR1 | 9-CDR2 | 9-CDR3 | YYYYY |
| KR20130067314 |  | CDR1 | 37-CDR2 | 37-CDR3 | 9-CDR1 | 9-CDR2 | 9-CDR3 | YYYYY |
| US20100254975 | Excel expor | CDR1 | 37-CDR2 | 37-CDR3 | 9-CDR1 | 9-CDR2 | 9-CDR3 | YYYYY |
| US20120177662 | Excel expor | CDR1 | 37-CDR2 | $37-$ CDR3 | 9-CDR1 | 9-CDR2 | 9-CDR3 | YYYYYY |
| US20120183561 |  | CDR1 | 37-CDR2 | 37-CDR3 | 9-CDR1 | 9-CDR2 | 9-CDR3 | YYYYY |
| US20130302354 | 6 | 37-CDR1 | 37-CDR2 | $37-\mathrm{CDR} 3$ | 9-CDR1 | $9-C D R 2$ | 9-CDR3 | YYYYY |
| US20140322209 | 6 | 37-CDR1 | 37-CDR2 | 37-CDR3 | 9-CDR1 | 9-CDR2 | 9-CDR3 | YYYYY |
| US20150086563 | 6 | 37-CDR1 | 37-CDR2 | 37-CDR3 | 9-CDR1 | 9-CDR2 | 9-CDR3 | YYYYY |
| US20170275365 | 6 | 37-CDR1 | 37-CDR2 | $37-\mathrm{CDR} 3$ | 9-CDR1 | $9-C D R 2$ | 9-CDR3 | Prrry |
| US8444981 | 6 | 37-CDR1 | 37-CDR2 | 37-CDR3 | 9-CDR1 | 9-CDR2 | 9-CDR3 | YYYYY |
| US8454961 | 6 | 37-CDR1 | 37-CDR2 | $37-$ CDR3 | 9-CDR1 | 9-CDR2 | 9-CDR3 | YYYYY |
| US8454962 | 6 | 37-CDR1 | 37-CDR2 | $37-\mathrm{CDR} 3$ | 9-CDR1 | 9-CDR2 | 9-CDR3 | YYYYY |
| US8871490 | 6 | 37-CDR1 | 37-CDR2 | $37-\mathrm{CDR} 3$ | 9-CDR1 | $9-C D R 2$ | 9-CDR3 | YYYYY |
| US9499620 | 6 | 37-CDR1 | 37-CDR2 | 37-CDR3 | 9-CDR1 | 9-CDR2 | 9-CDR3 | YYYYY |
| WO2010107752 | 6 | 37-CDR1 | 37-CDR2 | 37-CDR3 | 9-CDR1 | 9-CDR2 | 9-CDR3 | YYYYY |
| W02013078375 | 6 | 37-CDR1 | 37-CDR2 | 37-CDR3 | 9-CDR1 | 9-CDR2 | 9-CDR3 | PrYYY |
| W02017180587 | 6 | 37-CDR1 | 37-CDR2 | 37-CDR3 | 9-CDR1 | 9-CDR2 | 9-CDR3 | YYYYY |

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## US 8106170 B2

## CLAIMS

1. A composition comprising at least two immunoglobulins that are capable of specifically binding to Spike (S) protein of Severe Acute Respiratory Syndrome Coronavirus (SARS-Co-V) and neutralizing SAR S-CoV, wherein the first immunoglobulin comprises a heavy chain variable region comprising the amino acid sequence of SEQ ID NO: 4 and a light chain variable region comprising the amino acid seque nce of SEQ ID NO: 8, and wherein the second immunoglobulin comprises a heavy chain variable region comprising the amino acid sequence of SEQ ID NO: 6 and a light chain variable region comprising the amino acid sequence of SEQ ID NO: 10, and wherein the relative amounts of the at least two immunoglobulins are such that they exhibit a synergistic neutralizing activity.
2. The composition of claim 1 , wherein the immunoglobulins are capable of reacting with different, non-competing epitopes of the $S$ protein of SARS-CoV
3. The composition of claim 2 , wherein the immunoglobulins are capable of reacting with different, non-competing epitopes of amino acids 318-510 of the S protein (SEQ ID NO:115) of SARS-CoV
4. The composition of claim 1 , wherein at least one of the immunoglobulins is capable of reacting with an animal SARS-like CoV at a region corresponding to amino acids $318-510$ of the S protein (SEQ ID NO: 115) of SARS-CoV.

- A composition comprising at least two immunoglobulins that are capable of specifically binding to Spike (S) protein of Severe Acute Respiratory Syndrome Coronavirus (SARS-Co-V) and neutralizing SARS-CoV, wherein the first immunoglobulin comprises a heavy chain variable region comprising the amino acid sequence of SEQ ID NO: 4 and a light chain variable region comprising the amino acid sequence of SEQ ID NO: 8, and wherein the second immunoglobulin comprises a heavy chain variable region comprising the amino acid sequence of SEQ ID NO: 6 and a light chain variable region comprising the amino acid sequence of SEQ ID NO: 10, and wherein the relative amounts of the at least two immunoglobulins are such that they exhibit a synergistic neutralizing activity.

