# 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?

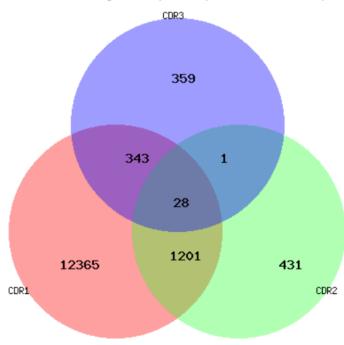
- Search & analyze as many as 250 sequences simultaneously
  - Apply saved (or newly-created) filters & views and create workflows that can be applied by non-expert users
  - Flexible filters, grouping and views allow interaction with specific sequence(s)
  - For the more detailed analysis or special 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**

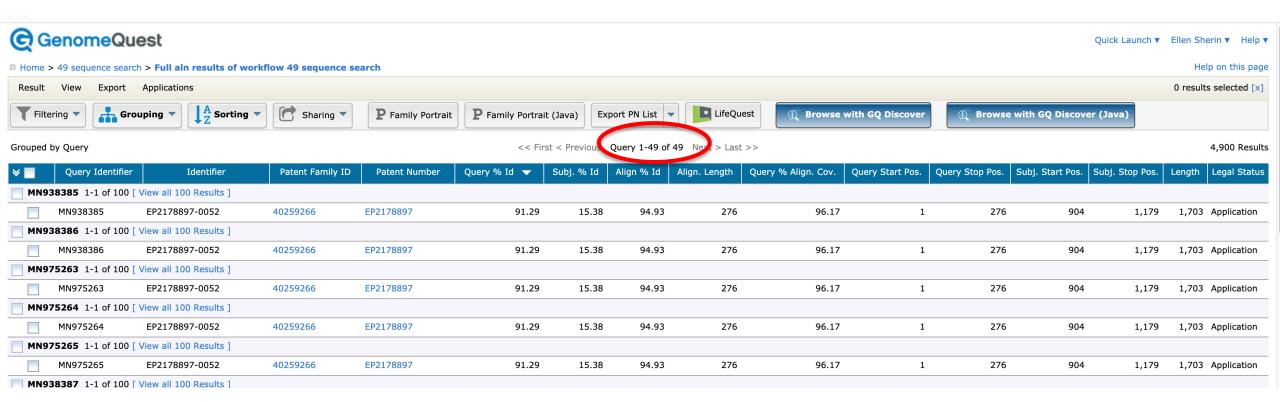
This is a Venn diagram of your 3 queries with hits to patents. The clickable numbers are the number of patents 1, 2 or 3 queries hit.



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
- □ repOrigin (5,475)
- oriT (5,051)
- regulatory1 (16,342)
- regulatory2 (1,387)
- lacZ (100,000)
- parE (52)
- parD (86)
- parC (27)
- parB (25)
- parA (25)
- aph (16,342)
- □ trfA (4,320)
- kanamycin\_PPT (24,995)

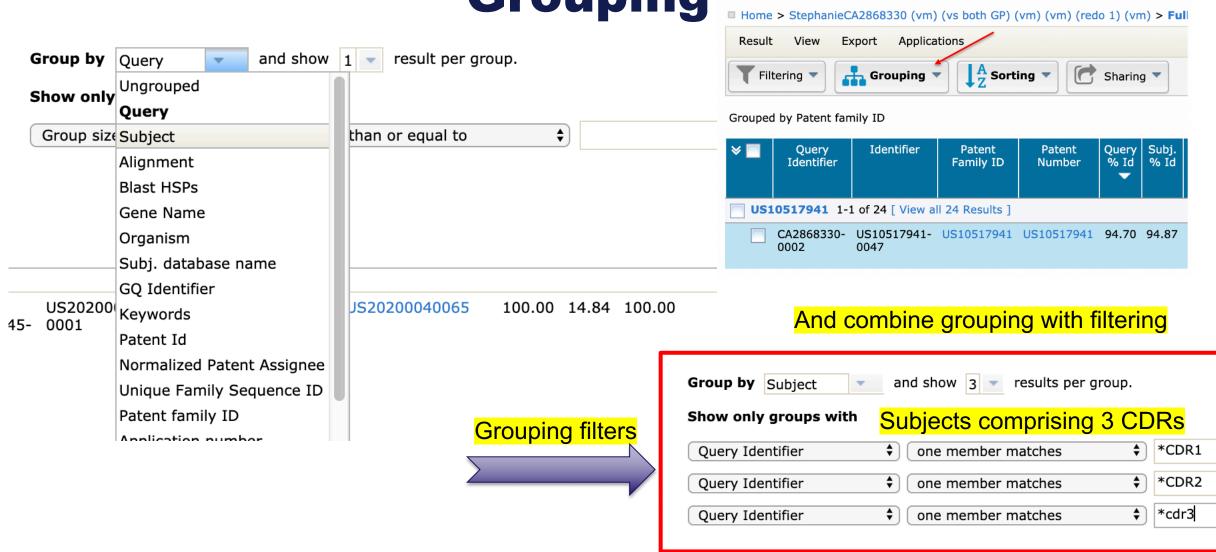
- Track the hit count for each query sequence
- Very visible if a query sequence is filtered out

- ▼ Query Sequence ID
  - HC-Ebola (74,100)
  - LC-Ebola (914,028)
  - HCDR1 (961,786)
  - HCDR2 (25,540)
  - HCDR3 (21)
  - LCDR1 (464,801)
  - LCDR2 (1,000,000)
  - LCDR3 (444,158)



### Grouping

**GenomeQuest** 

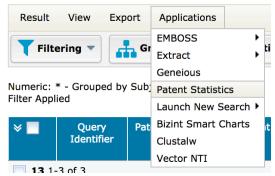


## Random Tip Select Families with Grouping & Date Filters

Group by Patent family ID	and show 3 vesults per gi	roup. New far	milies since 1	<mark>/1/20</mark>
Show only groups with				
Date of entry	earliest date is after	\$ 2020 \$ Ja	nuary 🗘 1 🕏	
Group by Patent family ID	and show 1 result per group.	Families with	<mark>new member</mark>	<mark>(s) since 1/2/20</mark>
Show only groups with				
Date of entry	• earliest date is before	\$ 2020 \$ January	<b>†</b> 1 <b>†</b>	- +
Date of entry	atest date is later than	\$ 2020 \$ January	<b>\$</b> 2 <b>\$</b>	- +

## Patent Statistics Report PN Level

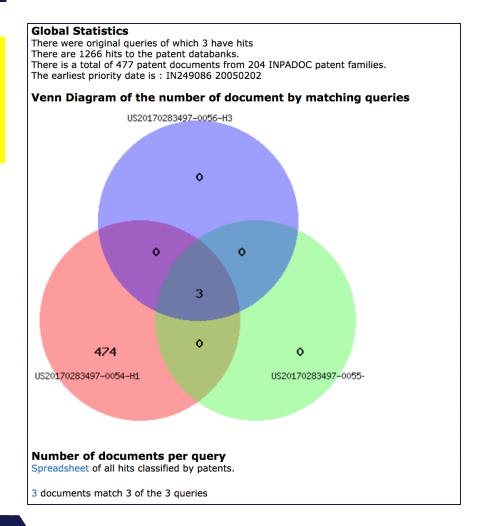
#### ■ Home > 6 CDR GP 80 > Full ain results of work



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

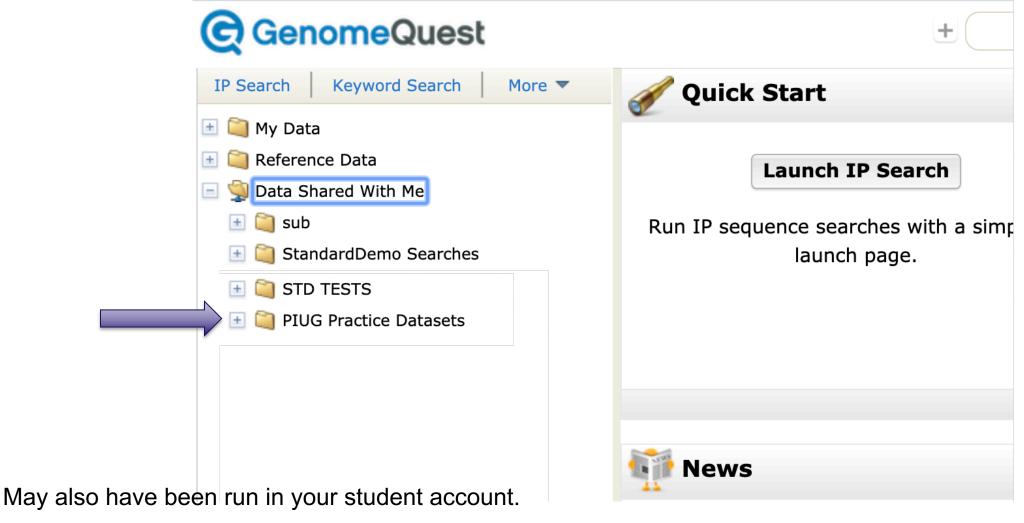
29 documents match 6 of the 6 queries

PATENT NUMBER	NB QUERIES	OUERY 1	OUERY 2	OUERY 3	OUERY 4	OUERY 5	QUERY 6	PATTERN
CA2754113	e NB QUERIES	37-CDR1	37-CDR2	37-CDR3	9-CDR1	9-CDR2	9-CDR3	YYYYYY
CA2754113 CA2851737	6	37-CDR1	37-CDR2	37-CDR3	9-CDR1	9-CDR2	9-CDR3	YYYYYY
CA2856866	6	37-CDR1	37-CDR2	37-CDR3	9-CDR1	9-CDR2	9-CDR3	YYYYYY
EP2408816	6	37-CDR1	37-CDR2	37-CDR3	9-CDR1	9-CDR2	9-CDR3	YYYYYY
JP2012520679	6	37-CDR1	37-CDR2	37-CDR3	9-CDR1	9-CDR2	9-CDR3	YYYYYY
JP2014140372	6	37-CDR1	37-CDR2	37-CDR3	9-CDR1	9-CDR2	9-CDR3	YYYYYY
JP2014140372 JP2015214563	6	37-CDR1	37-CDR2	37-CDR3	9-CDR1	9-CDR2	9-CDR3	YYYYYY
JP2015214363 JP2015505822	6	37-CDR1	37-CDR2	37-CDR3	9-CDR1	9-CDR2	9-CDR3	YYYYYY
JP5498566	<u> </u>	37-CDR1	37-CDR2		9-CDR1	9-CDR2	9-CDR3	YYYYYY
	<u> </u>	37-CDR1	37-CDR2	37-CDR3 37-CDR3	9-CDR1		9-CDR3	
JP5980384	<u> </u>					9-CDR2		YYYYYY
JP6203740	Ь	37-CDR1	37-CDR2	37-CDR3	9-CDR1	9-CDR2	9-CDR3	YYYYYY
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	YYYYYY
KR20130067314		CDR1	37-CDR2	37-CDR3	9-CDR1	9-CDR2	9-CDR3	YYYYYY
US20100254975	Excel exp	Ort CDR1	37-CDR2	37-CDR3	9-CDR1	9-CDR2	9-CDR3	YYYYYY
US20120177662		CDR1	37-CDR2	37-CDR3	9-CDR1	9-CDR2	9-CDR3	YYYYYY
US20120183561		CDR1	37-CDR2	37-CDR3	9-CDR1	9-CDR2	9-CDR3	YYYYYY
US20130302354	6	37-CDR1	37-CDR2	37-CDR3	9-CDR1	9-CDR2	9-CDR3	YYYYYY
US20140322209	6	37-CDR1	37-CDR2	37-CDR3	9-CDR1	9-CDR2	9-CDR3	YYYYYY
US20150086563	6	37-CDR1	37-CDR2	37-CDR3	9-CDR1	9-CDR2	9-CDR3	YYYYYY
US20170275365	6	37-CDR1	37-CDR2	37-CDR3	9-CDR1	9-CDR2	9-CDR3	YYYYYY
US8444981	6	37-CDR1	37-CDR2	37-CDR3	9-CDR1	9-CDR2	9-CDR3	YYYYYY
US8454961	6	37-CDR1	37-CDR2	37-CDR3	9-CDR1	9-CDR2	9-CDR3	YYYYYY
US8454962	6	37-CDR1	37-CDR2	37-CDR3	9-CDR1	9-CDR2	9-CDR3	YYYYYY
US8871490	6	37-CDR1	37-CDR2	37-CDR3	9-CDR1	9-CDR2	9-CDR3	YYYYYY
US9499620	6	37-CDR1	37-CDR2	37-CDR3	9-CDR1	9-CDR2	9-CDR3	YYYYYY
WO2010107752	6	37-CDR1	37-CDR2	37-CDR3	9-CDR1	9-CDR2	9-CDR3	YYYYYY
WO2013078375	6	37-CDR1	37-CDR2	37-CDR3	9-CDR1	9-CDR2	9-CDR3	YYYYYY
WO2017180587	6	37-CDR1	37-CDR2	37-CDR3	9-CDR1	9-CDR2	9-CDR3	YYYYYY





#### **Workshop Searches Here**



## **Practice: Grouping & Patent Statistics**

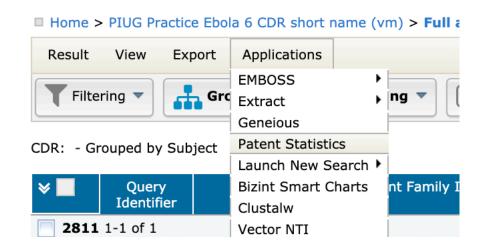
#### **Basic:** PIUG Practice Ebola LC CDRs 10k (vm)

- 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)

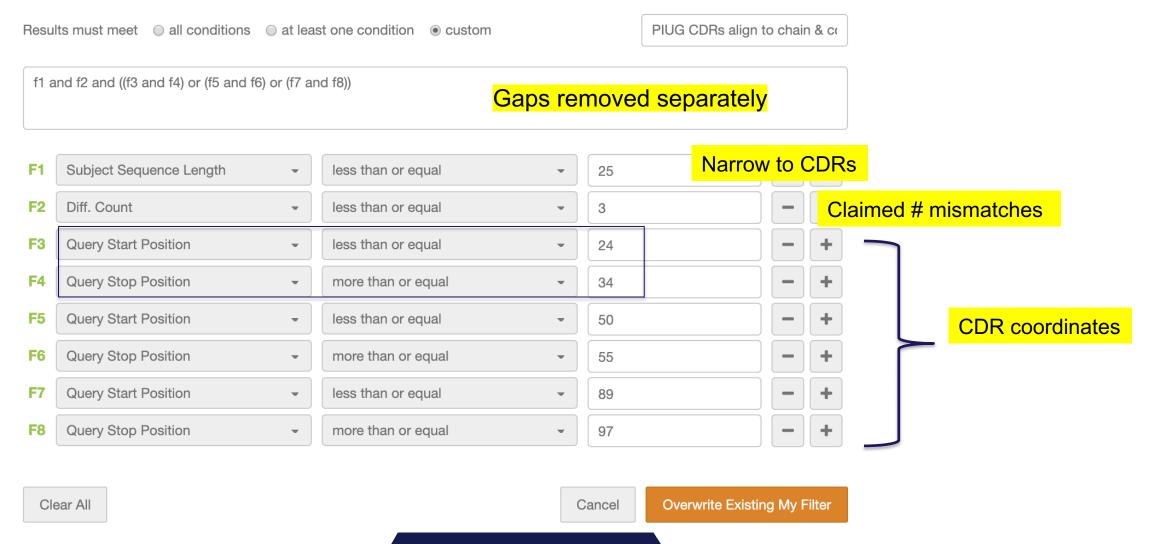
- 1. Go directly to search results
- Create your own grouping filter to narrow to chains comprising all 3 HC CDRs, then chains comprising all 3 LC CDRs.
- Experiment with Patent Statistics to find PNs with all 6 CDRs



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





# Multiple Query Sequence Analysis Working with Chains & CDRs

#### **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 •	
Query number of gaps 🕈 less than or equal to	<b>†</b> ) 0
Subj. number of gaps 🗘 less than or equal to	<b>†</b> 0
Length   greater than	\$ 50

Match to only CDRs	
Show results that meet all conditions \$	
Query number of gaps 🗘 less than or equal to	<b>\$</b> 0
Subj. number of gaps 💠 less than or equal to	<b>\$</b> 0
Length	\$ 40

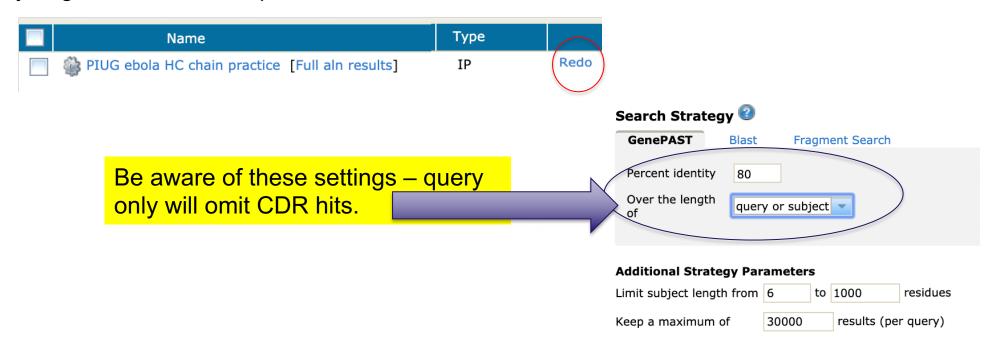
The key is the length field
This means "length of hit sequence"



#### **Practice - Query Sequence is Chain**

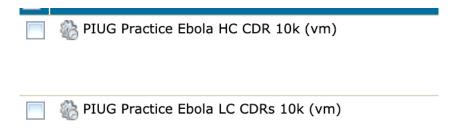
#### **PIUG Practice HC full chain (vm)**

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 10k hits both times. How many results do you get for each set of parameters?



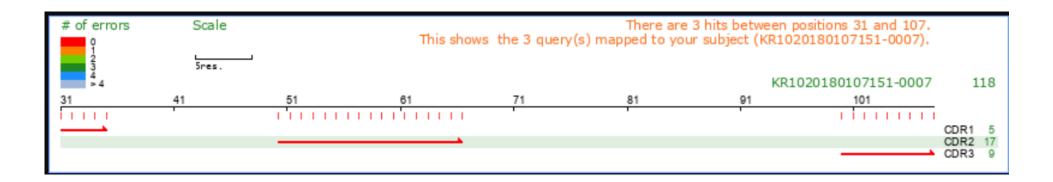
## Let's get some CDR searches going

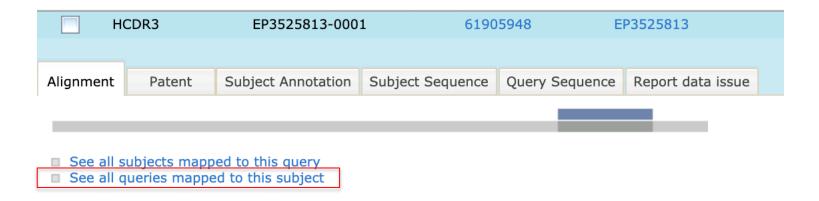
Click REDO for the following searches:

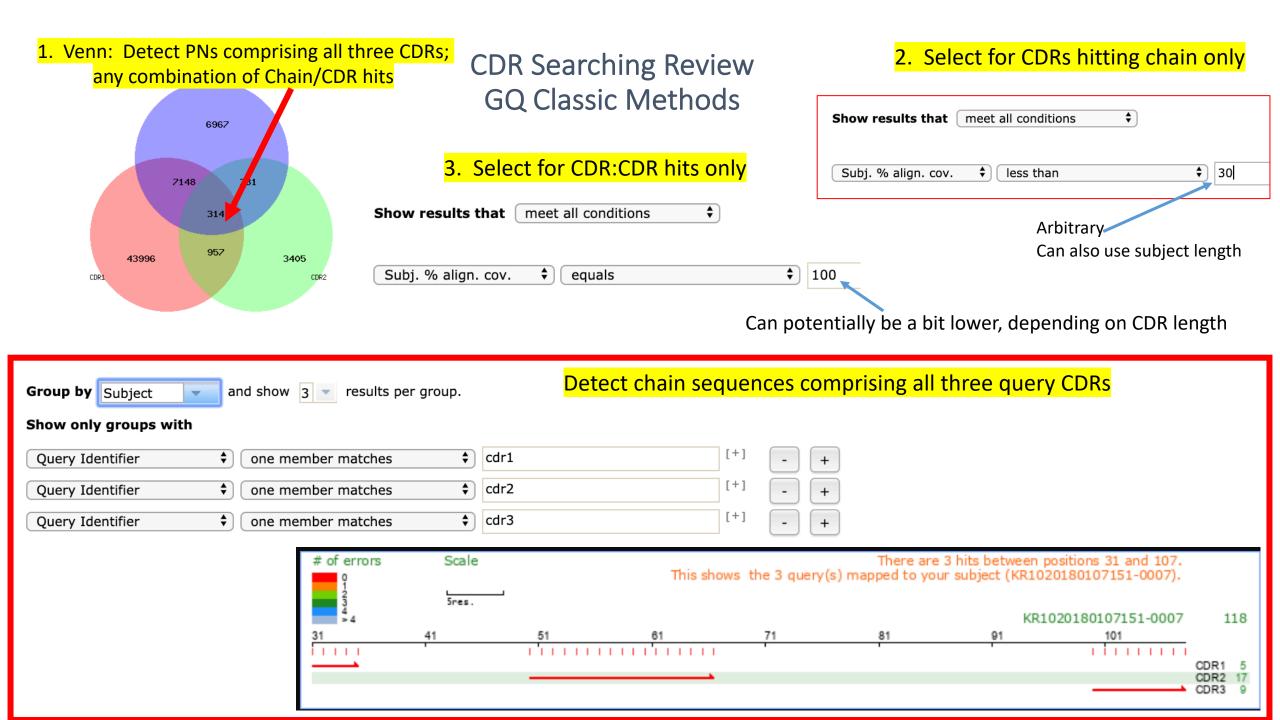


You are welcome to change the parameters, or just leave them alone for now. We'll use them later.

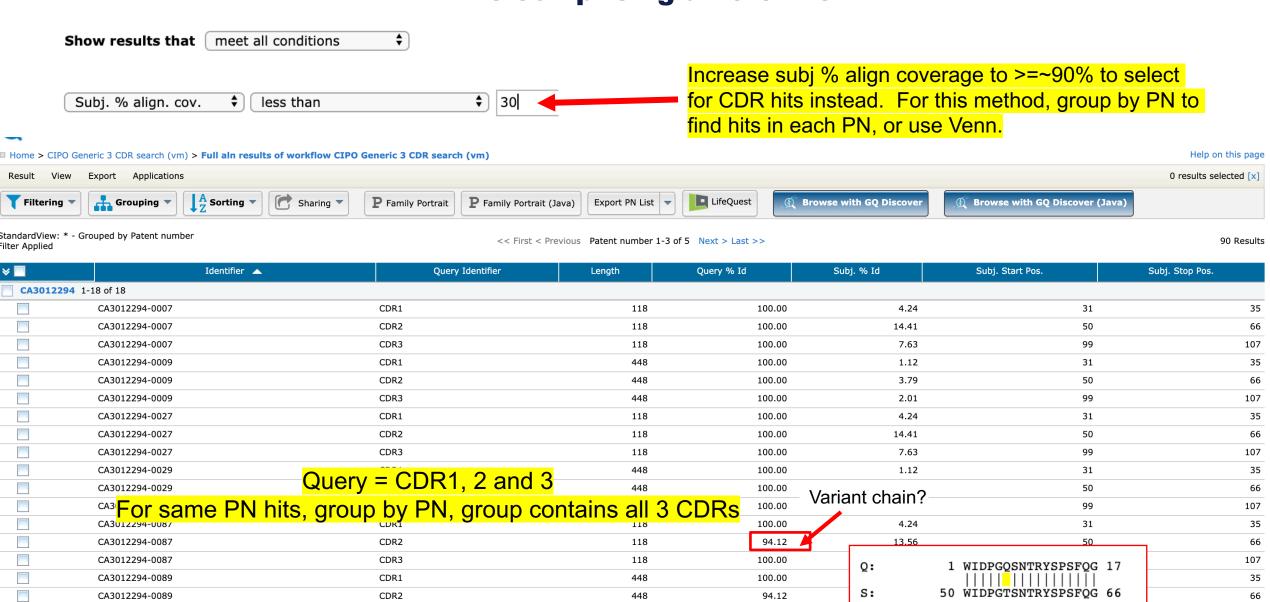
## **Visualizing CDRs**







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



448

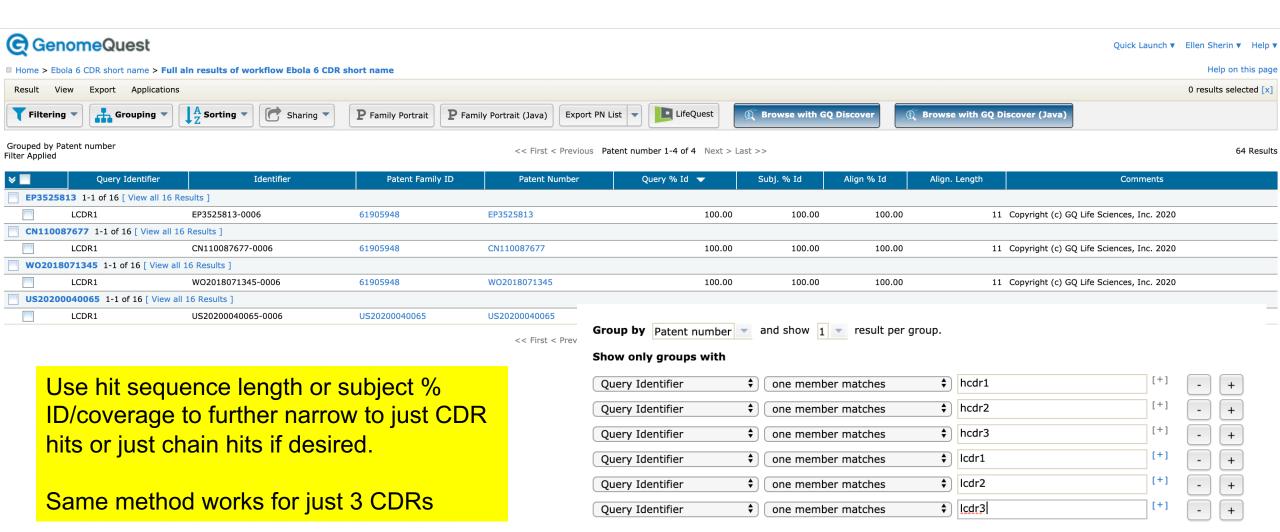
100.00

107

CA3012294-0089

CDR3

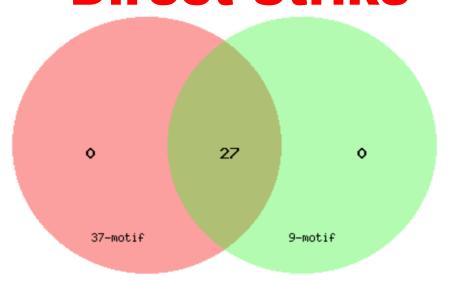
## Search for PNs comprising all 6 Query CDRs





# 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

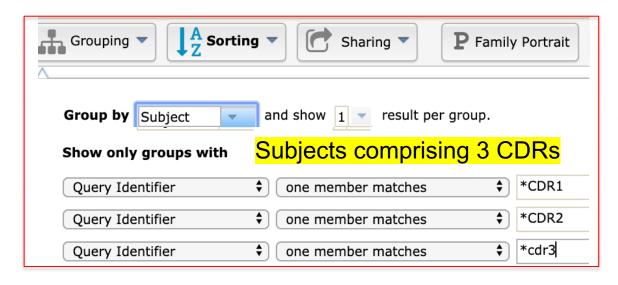
>37-CDR1
DLSIH
>37-CDR2
GFDPQDGETIYAQKFQG
>37-CDR3
GSSSSWFDP

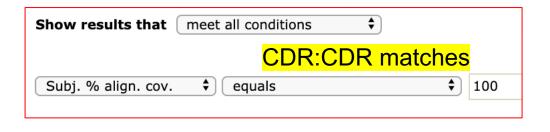


## Method 2: Group & Filter, GQ Classic (Review)

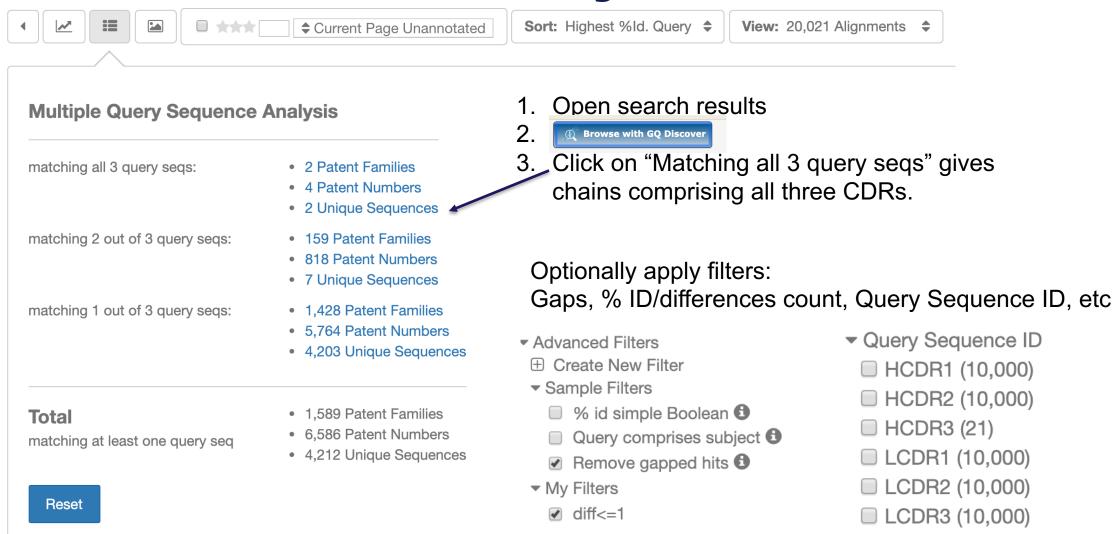


Select for subjects comprising all three CDRs (or a subset of CDRs) or for CDR:CDR matches instead (or sequentially).



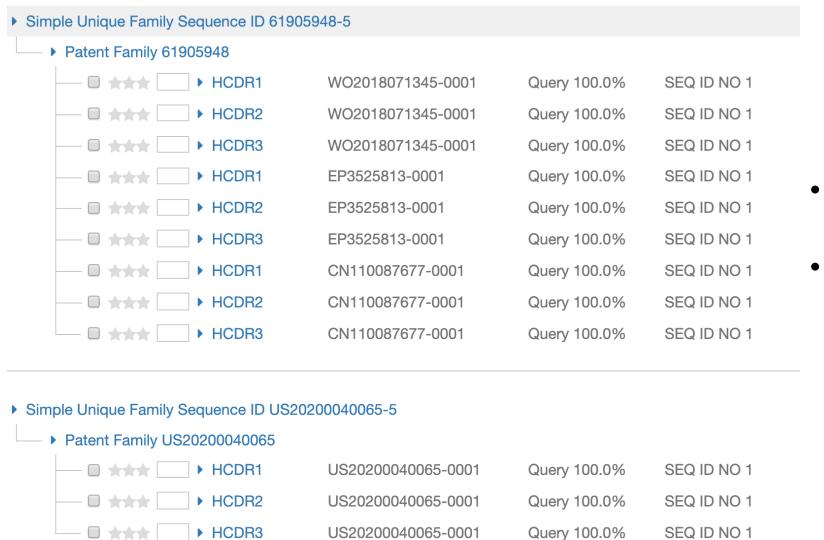


## Method 3: 3 click analysis in GQ Discover





## What are "Unique Sequences"?



- This is the UFS we use regularly
- It is the identical sequence, segregated by patent family.



#### Our upcoming release....

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

#### **My Column Groups**

- ⊕ Select Displayed Columns
- Saved Views

#### **Highlight Text**

Highlight all tex

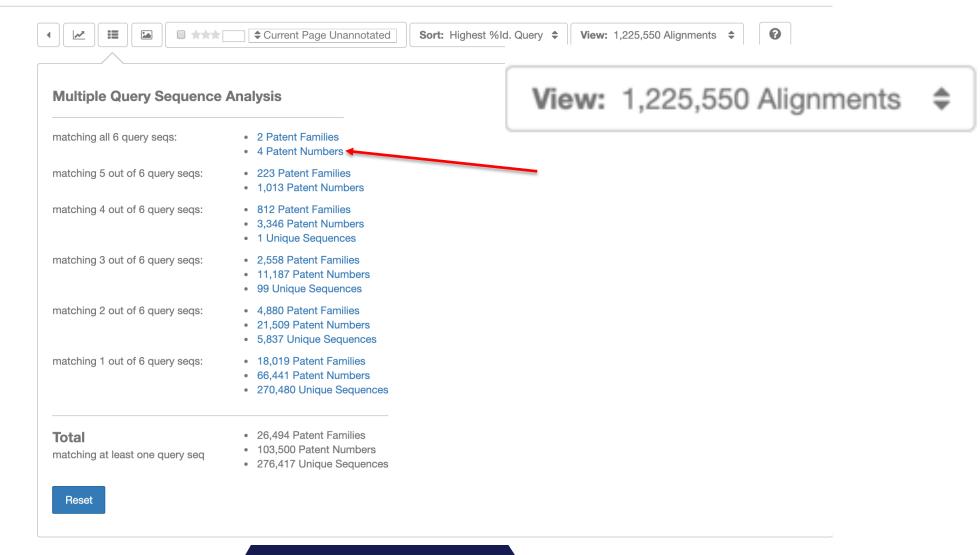
#### **Filter Text**

Soamh all toy

- ▼ Query Sequence ID
- HCDR1 (300,000)
- HCDR2 (25,529)
- HCDR3 (21)
- LCDR1 (300,000)
- LCDR2 (300,000)
- 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
- ▼ Variation Filters
- ⊕ Create New Variation Filter
- Global Filters
- ▶ Result-specific Filters
- ▶ Variation Landscape





#### From 1.2 million to 64 results



#### **My Column Groups**

- ⊕ Select Displayed Columns
- Saved Views

#### **Highlight Text**

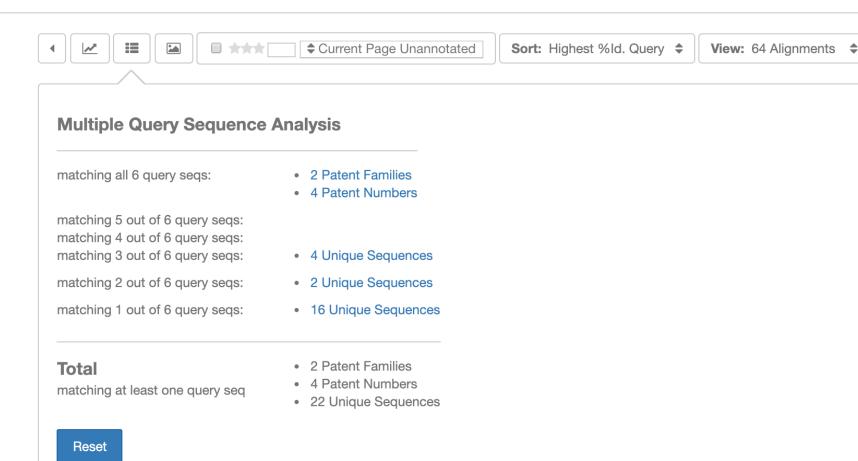
Highlight all text

#### Filter Text

Search all text

- ▼ Query Sequence ID

- LCDR1 (12)
- LCDR2 (8)
- LCDR3 (16)
- ▶ Patent Numbers
- ▶ Sequence Databases
- ▶ Annotation Filters
- ▶ Patent Authorities
- ▶ Extended Legal Status

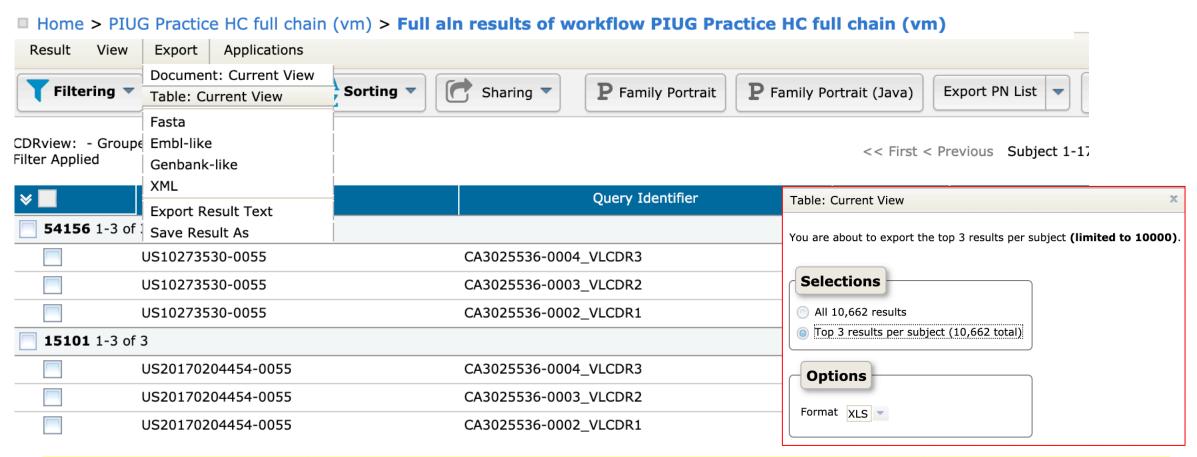




8

# 3 CDR Report Creation GQ Classic

**GenomeQuest** 



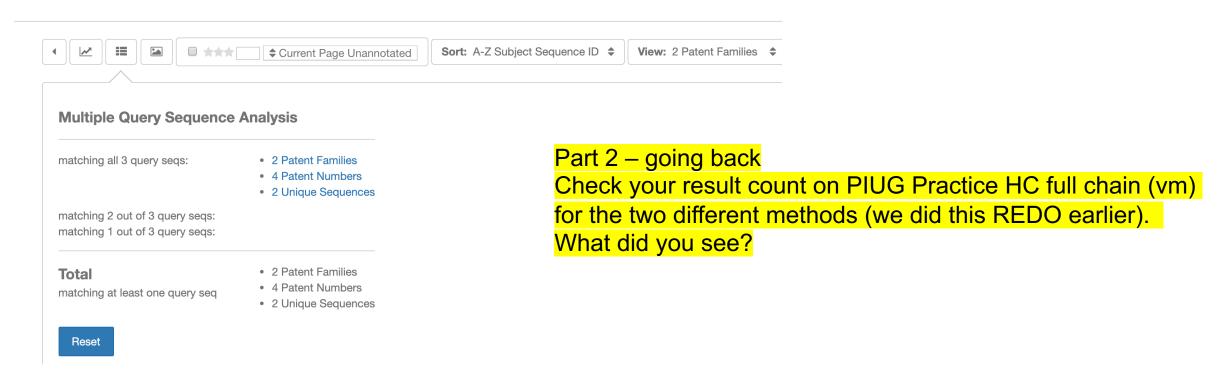
You could even make group size =1, then export top 1 result/subject, given that each subject comprises the three CDRs



## **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.



## Moving on to some claims

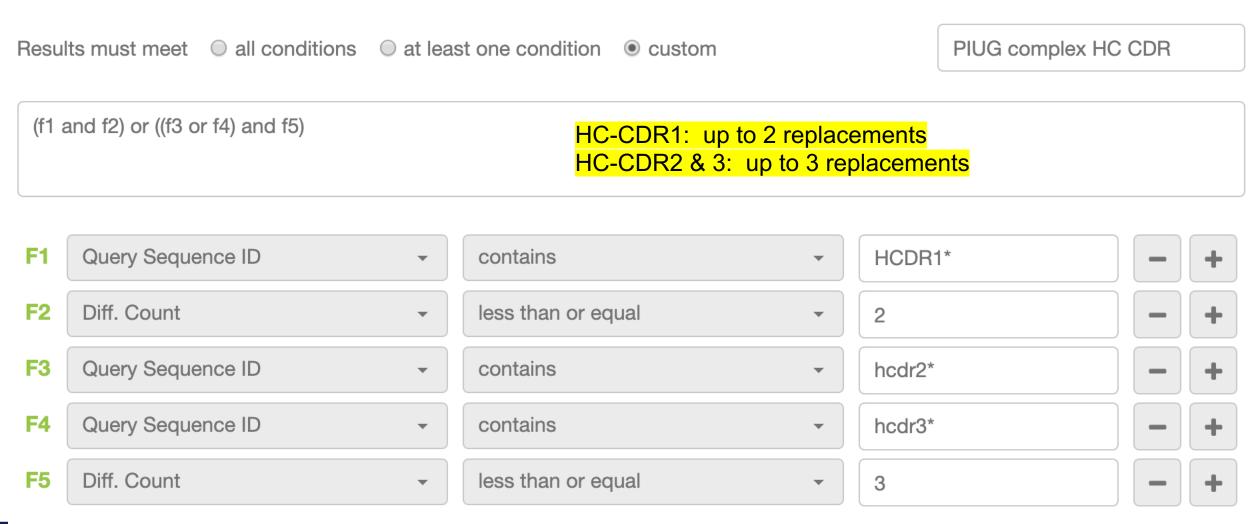


#### **HC Analysis**

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, XI1, 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...

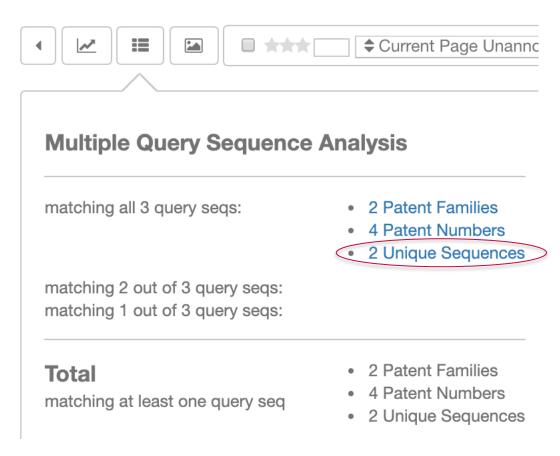
# Custom Boolean Replacement Count and Query Identifier



### **Comprising all three**

L 11000000040005

#### We dodged a bullet!



US20200040065		
— □ ★★★ ► HCDR1-WO2018071345-0003	Query 100.0%	US20200040065-0001
— □ → HCDR2-WO2018071345-0004	Query 100.0%	US20200040065-0001
— □ ★★★	Query 100.0%	US20200040065-0001
► EP3525813		
— □ ★★★	Query 100.0%	EP3525813-0001
— □ ★☆★	Query 100.0%	EP3525813-0001
— □ ★★★	Query 100.0%	EP3525813-0001
CN110087677		
— □ ★★★	Query 100.0%	CN110087677-0001
— □ ★★★	Query 100.0%	CN110087677-0001
— □ ★★★	Query 100.0%	CN110087677-0001
WO2018071345		
— □ → HCDR1-WO2018071345-0003	Query 100.0%	WO2018071345-0001
— □ → HCDR2-WO2018071345-0004	Query 100.0%	WO2018071345-0001
— □ → HCDR3-WO2018071345-0005	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 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, XI1, 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, XI1, 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, XI1, 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, XI1, 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



#### WO2018071345

#### LC Claim Section, Claim 6

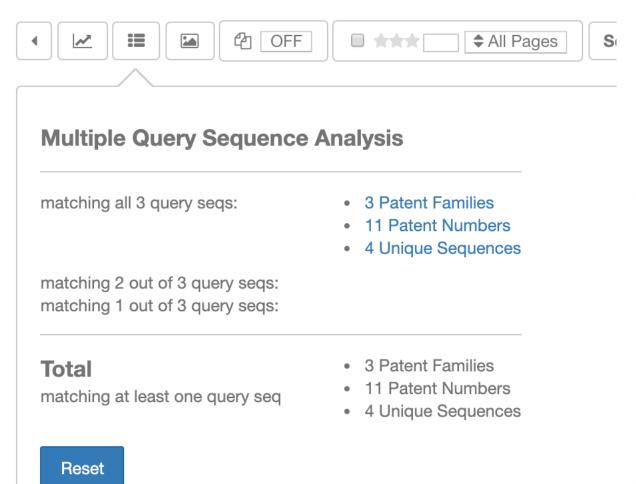
wherein the VL comprises light chain complementarity determining regions CDRL1, CDRL2, and CDRL3, wherein CDRL1 comprises SEQ ID NO: 6, or SEQ ID NO: 6 with one, two, or three single amino acid substitutions; wherein CDRL2 comprises SEQ ID NO: 7, or SEQ ID NO: 7 with one, two, or three single amino acid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

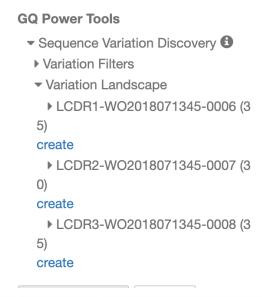
Show results that meet all conditions \$	First the regular search
No. diff	<b>\$</b>
Subj. number of gaps 💠 equals	<b>†</b> 0
Query number of gaps 🕏 equals	<b>†</b> ) 0



# **GQ Discover How to Identify Variations**



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



## Variation Landscape Overview Narrow Resultset

RASOSISNNL A

LC-CDR1

Query position	Variation type	Description
11	Replacement	A11N (14)

AASNLA

LC-CDR2

Query position	Variation type	Description

No variations found

QQHNTLPLT

LC-CDR3

Query 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

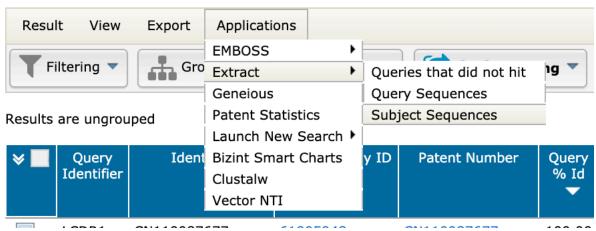
Let's take it further – Let's create a landscape for our three CDR regions.

Use chain as query here



#### **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.

#### In "my data"



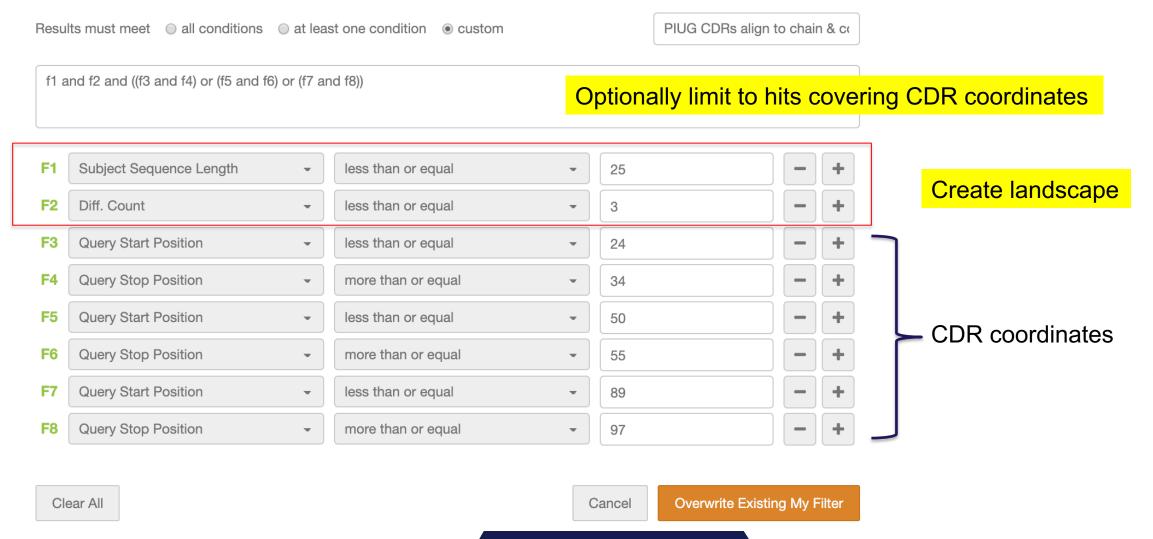


## Normal GQ Search vs vDB

Result Name PIUG Ebola LC chain vs my 3CDR db	Send E-mail on completion				
Compare to both nucleotide and protein databases					
Include variation analysis capability					
form to Street and Street		Use GQ view to ide	entity CDR po	sitions for nex	kt step
Search Strategy GenePAST Blast Fragment Search					
		Identifier	Query Start Pos.	Query Stop Pos.	
Percent identity 65		Identinei	Query Start Fos.	Query Stop Fos.	
Over the length of query or subject		WO2018071345-0006	24	34	
		WO2018071345-0008	89	97	
Additional Strategy Parameters					
Limit subject length from 6 to 1000 residues		WO2018071345-0007	50	55	
Keep a maximum of 250000 results (per query)					
Subject Databases ②					
▶ Apply filters to subject databases					
Nucleotides	Prote	ins		vDR shows i	ıp in My Data o
→ Patents	<b>±</b> [	Patents			
Reference Data	± [			Data Shared	with Me
■ Data Shared With Me	= [	•			
My Data		BGN			
		ebola CDR nogap vdb ebolaWTvdb			
		piug ebola comprise all 3  PIUG Biotech PIUG LC 3 cdr db  PIUG WO2018071345 HC full chain only			
		PIUG W02018071345 LC full chain			



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





## **Create & Export Variation Landscape**

- □ FIUG <=3 UIII LU</p>
- ✓ PIUG CDRs align to chain & cor
- PIUG complex HC CDR
- PIUG Ebola chain query
- PIUG Ebola LC query
- subtilase cas family dedupe
- WO2010056640-subtl demo

#### **GQ Power Tools**

- ▼ Sequence Variation Discovery
- ▼ Variation Filters
  - **Example 2** Create New Variation Filter
- Global Filters
- Result-specific Filters
- ▼ Variation Landscape
  - ▶ LC-Ebola (43,052) create



#### **Variation Landscape Summary Table**

r	-	_	-	۰	
ı		٠		-1	
н	4	_	٠	. І	

Query position	Variation type	Description					
24	Replacement	R24K(11), R24Q(354)					
<u>25</u>	Replacement	A25P(4), A25T(2)					
<mark>26</mark>	Replacement	S26N(16), S26Q(9)					
<mark>27</mark>	Replacement	Q27E(31), Q27H(5), Q27K(3), Q27P(10), Q27R(11)					
<mark>28</mark>	Replacement	S28A(76), S28D(517), S28G(2841), S28N(17), S28P(6), S28R(15), S28T(62), S28V(44), S28Y(14)					
<mark>29</mark>	Replacement	I29L(19), I29M(27), I29S(16), I29V(2707), I29W(1), I29X(10)					
30	Replacement	S30A(32), S30F(43), S30G(186), S30H(4), S30I(24), S30K(64), S30L(6), S30N(127), S30R(111), S30T(19), S30V(10), S30W(1), S30Y(85)					
<mark>31</mark>	Replacement	N31A(4), N31D(71), N31E(16), N31F(31), N31G(50), N31H(66), N31I(30), N31K(18), N31R(333), N31S(10307), N31T(295), N31V(28), N31Y(79), N31Z(3)					
<mark>32</mark>	Replacement	N32A(60), N32C(6), N32D(263), N32F(3959), N32G(2), N32H(150), N32I(2), N32L(109), N32Q(92), N32R(79), N32S(340), N32T(14), N32W(5671), N32Y(3378)					
<mark>33</mark>	Replacement	L33 <u>V(52)</u>					
<mark>34</mark>	Replacement	A34G(11), A34H(828), A34I(5), A34L(14), A34N(977), A34Q(27), A34S(37), A34T(2), A34V(31), A34X(3)					
35	Replacement	W35T(18), W35Z(16)					
39	DIQMTQSPSS LSASVGDTVT ITCRASQSIS NNLAWYQQRP RRAPQLLIYA	R39 <u>K(</u> 17)					
	ASNLASGVPS RFSGSGSGTD FTLTISSLQA EDFAAYYCQQ HNTLPLTFGG	L46 <u>A(</u> 1), L46P(111), L46R(1), L46S(1), L46T(1)					
47	GTKVEI	L47A(1), L47K(4), L47W(119)					
48		148 <u>A(</u> 4), 148L(1), 148S(4), 148V(24)					
49	Replacement	Y49 <u>A(</u> 18), Y49D(3), Y49F(2), Y49G(8), Y49H(1), Y49I(8), Y49K(1), Y49N(9), Y49P(15), Y49Q(1), Y49S(7), Y49V(4)					
<u>50</u>	Replacement	A50D(186), A50G(483), A50H(3), A50K(78), A50L(68), A50Q(164), A50R(418), A50S(182), A50T(39), A50V(12), A50W(3) A51C(2), A51D(2), A51E(2), A51F(2), A51F(2), A51G(4), A51H(5), A51I(26), A51K(3), A51L(2), A51M(2), A51N(2), A51P(367), A51Q(2), A51R(2), A51S(39), A51					
<mark>51</mark>	Replacement	T(1828), A51V(8), A51W(2), A51X(1), A51Y(2)					
<mark>52</mark>	Replacement	S52A(12), S52F(52), S52I(1), S52K(9), S52M(36), S52R(34), S52T(1046)					
<mark>53</mark>	Replacement	N53D(30), N53F(43), N53G(3), N53I(8), N53K(90), N53L(34), N53P(36), N53R(10), N53S(50), N53T(165), N53Y(9)					
<del>54</del>	Replacement	L54E(3), L54G(3), L54I(3), L54N(3), L54Q(5), L54R(98), L54T(6), L54V(7)					
<mark>55</mark>	Replacement	A55D(132), A55E(8012), A55G(61), A55H(64), A55I(21), A55K(101), A55P(6), A55Q(1074), A55R(59), A55S(3), A55T(1), A55X(7), A55Y(37)					
56	Repla	S56A(58). S56C(2). S56D(1358). S56E(17). S56F(141). S56H(2), S56I(17), S56K(19), S56L(5), S56M(2), S56N(25), S56P(26), S56Q(6), S56R(39), S56					
57	Remember the ALA in HC claims						
58 60	Repli any of the recited positions; if four	nd we'd build appropriate					
88	<u> </u>						
<mark>89</mark>	Repli variation filters						
<mark>91</mark>	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	T93A(9), T93E(401), T93H(12), T93K(15), T93N(135), T93S(84), T93V(4), T93Y(2)					
<mark>94</mark>	Replacement	L94A(6), L94D(73), L94F(64), L94H(3), L94I(33), L94N(73), L94P(4), L94S(68), L94T(105), L94W(116), L94Y(551)					
<del>96</del>	Replacement	L96A(8), L96F(98), L96H(8), L96I(12), L96P(236), L96R(45), L96W(1174), L96X(3), L96Y(4067)					
98	Replacement	F98 <u>T(</u> 4)					
100	Replacement	G100 <u>S(</u> 5)					
102	Replacement	T102C(8)					

# Multiple Query Sequence Analysis Combinations of Components Constructs & Elements

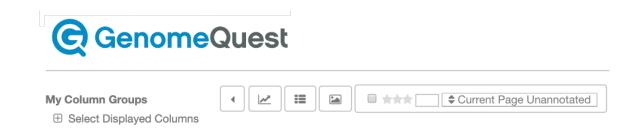
# Find Component Combinations Interactively in GenomeQuest

**GQ Classic** 



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

**GQ** Discover



- 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**

Compone	Components: * - Grouped by Query											,127 Results						
<b>* </b>	Query Identifier	Identifier	Patent Family ID	Patent Number	Query % Id	Subj. % Id	Align % Id	Align. Length	Query Start Pos.		Subj. Start Pos.	Subj. S Pos.		atent SEQ ID NO	Patent Sequence Location		Title	
parE	1-1 of 52 [ View a	ll 52 Results ]		•					·									
		US20190348154- 153544	56014840	US20190348154	100.00	100.00	100.00	312	1	312	1	. :	312	153,544 c	claim: 1; 4	STABLE PAN-GENOMES AND THEIR USE		
parD	1-1 of 86 [ View a	ll 86 Results ]																
		US20190348154- 153543	56014840	US20190348154	100.00	100.00	100.00	252	1	252	1		252	153,543 c	claim: 1; 4	STABLE PAN-GENOMES AND THEIR USE		
parC	1-1 of 27 [ View a	ll 27 Results ]																
		US20190348154- 153542	56014840	US20190348154	100.00	100.00	100.00	294	1	294	1	. :	294	153,542 c	claim: 1; 4	STABLE PAN-GENOMES AND THEIR USE		
trfA	1-1 of 4,320 [ View	all 4,320 Results ]																
		US20190348154- 54020	56014840	US20190348154	100.00	100.00	100.00	1,149	1	1,149	1	1,:	149	54,020 c	claim: 1; 4	STABLE PAN-GENOMES AND THEIR USE		
parB	1-1 of 25 [ View a	Il 25 Results ]																
		US20190348154- 153541	56014840	US20190348154	100.00	100.00	100.00	534	1	534	1	. !	534	153,541 c	claim: 1; 4	STABLE PAN-GENOMES AND THEIR USE		
lacZ	1-1 of 100,000 [ V	iew all 100,000 Resu	ilts ]															
	lacZ	JP6011759-0015	48187192	JP6011759	100.00	100.00	100.00	21	1	21	1		21		probable disclosure (not found by automated parsing)	Silencing suppressor and method for obtaini	ng the	

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



## GQ Classic Group & Filter – Direct Strike (What we did with CDR searches)

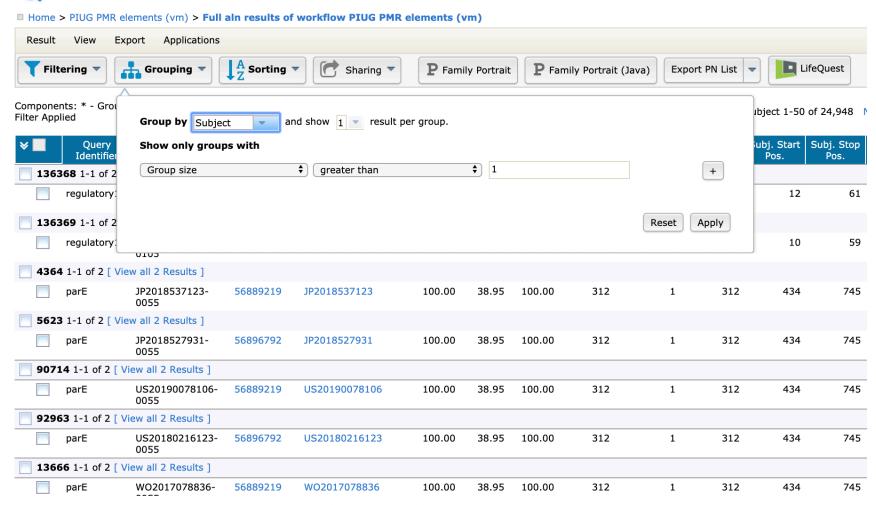
Group by Subject	and show 1 result per grou	p.	
Show only groups with			
Query Identifier	one member matches	♦ lacZ	[+] - +
Query Identifier	one member matches	<b>♦</b> oriT	[+] - +
Query Identifier	one member matches	regulatory1	[+] - +
Query Identifier	one member matches	<b>‡</b> trfA	[+] - +
			Reset Apply

Works perfectly and is highly specific. Excellent for CDRs



# GQ Classic Broader Search (Pivot Setup)

#### **GenomeQuest**

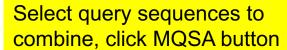


Here we are just filtering by group size, not specific query sequences comprised by a subject.

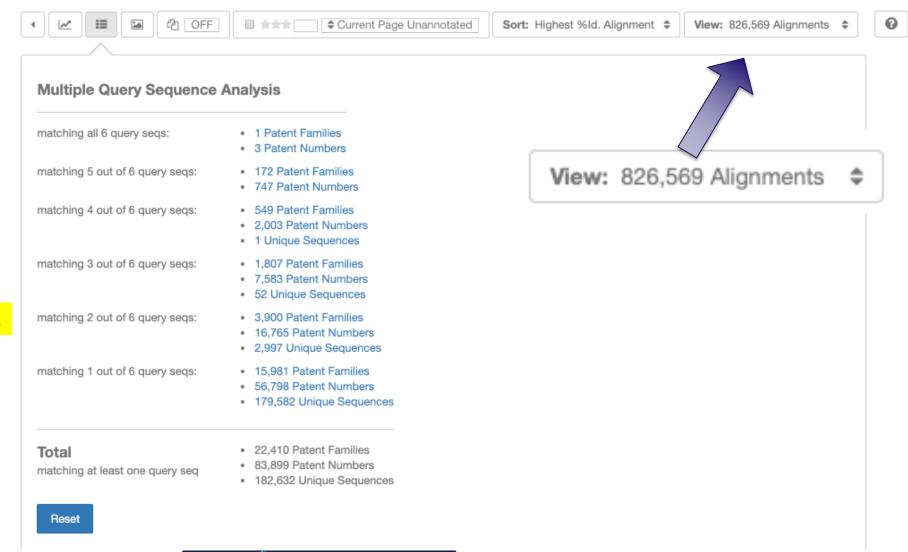
Next step (after filtering for % identity or any other attributes), is to export as Excel, and then prepare a pivot table.



# **GQ Discover Multiple Query Sequence Analysis**

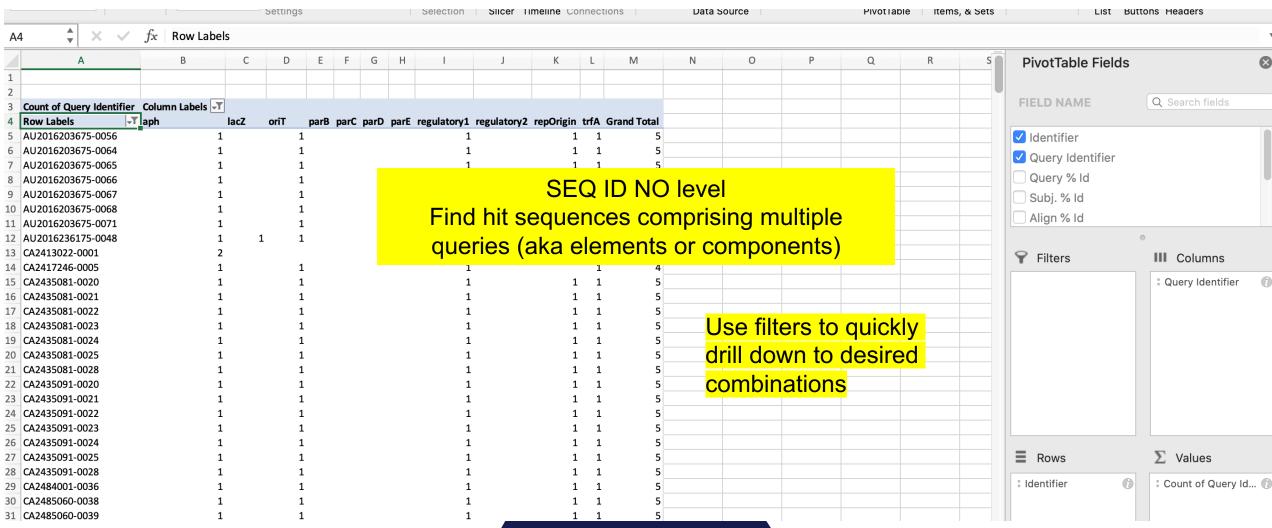


- ▼ Query Sequence ID
- repOrigin (2,696)
- oriT (3,896)
- regulatory1 (16,089)
- regulatory2 (1,332)
- lacZ (88,318)
- parE (47)
- parD (77)
- □ parC (26)□ parB (23)□ parB (23)
- parA (0)
- aph (16,089)
- □ trfA (4,304)
- kanamycin\_PPT (18,752)





## 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?

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Stephen.Allen@aptean.com
Ellen.Sherin@aptean.com

# aptean

#### WO2018071345A1

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, XI1, 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.

- 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, XI1, 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.

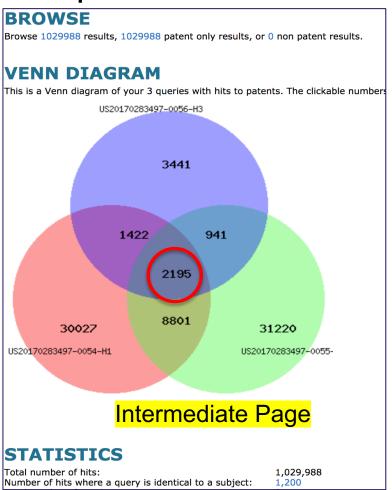
- Search chains & CDRs GenePast, 65% over query
- 2. Group for chains comprising all 3, make vdb
- 3. Search against these chains and do vm analysis. Since they already comprise all 3 I don't have to annotate them, so I can do the variants and not out the ones with non-specified mismatches.
- 4. The 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**

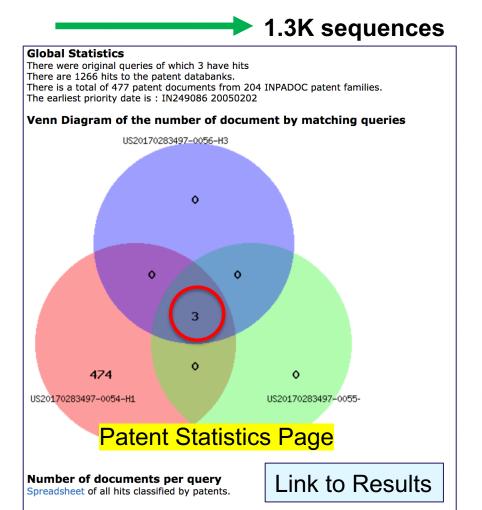


# Results Pre & Post filtering Patent-Level Grouping

#### 1MM sequences



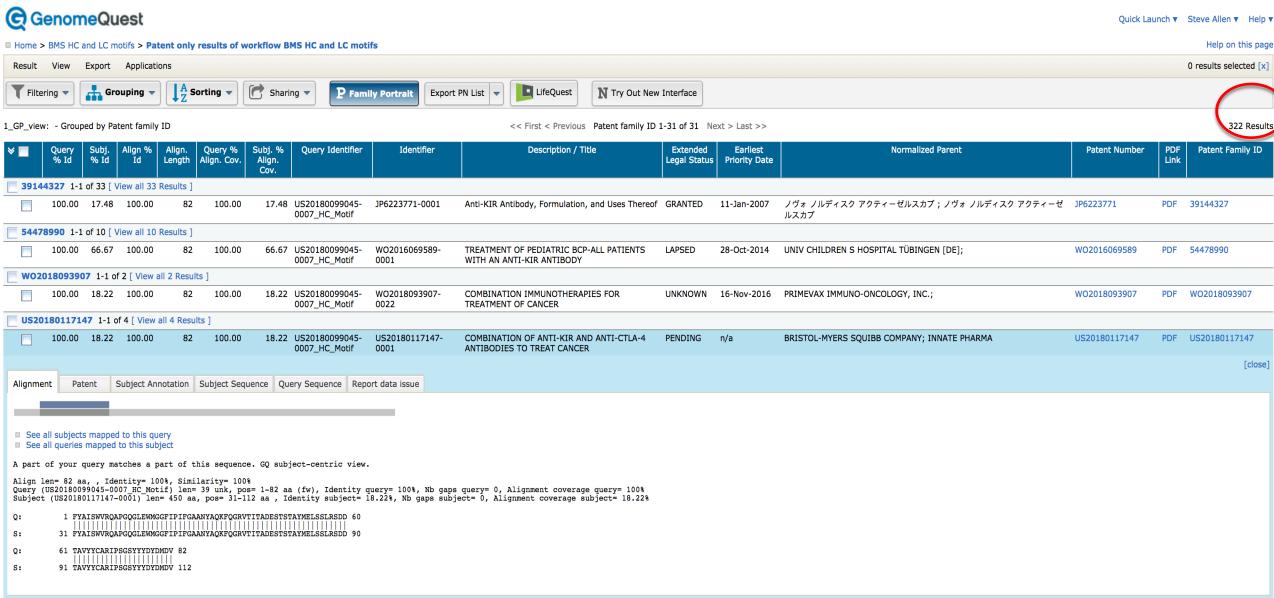
### Filter



3 documents match 3 of the 3 queries



## **Motif – Targeted Results**

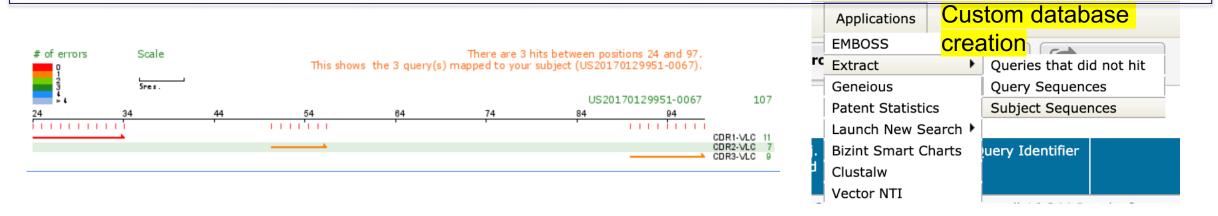


**US20180099045** 1-1 of 4 [ View all 4 Results ]

[close]

# 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



## **◯** GenomeQuest

# **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

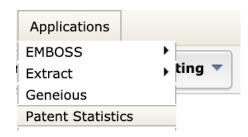
165 documents match 5 of the 11 queries

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 queries

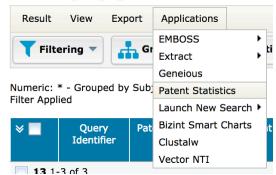


This is on the patent number level...a little later we will talk about identifying hit sequences comprising different combinations of query sequences



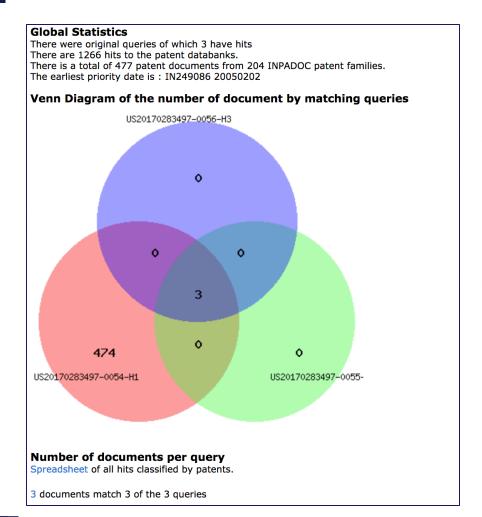
# Patent Statistics Report PN Level

#### ■ Home > 6\_CDR\_GP\_80 > Full ain results of work



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	YYYYYY
CA2851737	6	37-CDR1	37-CDR2	37-CDR3	9-CDR1	9-CDR2	9-CDR3	YYYYYY
CA2856866	6	37-CDR1	37-CDR2	37-CDR3	9-CDR1	9-CDR2	9-CDR3	YYYYYY
EP2408816	6	37-CDR1	37-CDR2	37-CDR3	9-CDR1	9-CDR2	9-CDR3	YYYYYY
JP2012520679	6	37-CDR1	37-CDR2	37-CDR3	9-CDR1	9-CDR2	9-CDR3	YYYYYY
JP2014140372	6	37-CDR1	37-CDR2	37-CDR3	9-CDR1	9-CDR2	9-CDR3	YYYYYY
JP2015214563	6	37-CDR1	37-CDR2	37-CDR3	9-CDR1	9-CDR2	9-CDR3	YYYYYY
JP2015505822	6	37-CDR1	37-CDR2	37-CDR3	9-CDR1	9-CDR2	9-CDR3	YYYYYY
JP5498566	6	37-CDR1	37-CDR2	37-CDR3	9-CDR1	9-CDR2	9-CDR3	YYYYYY
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	YYYYYY
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	YYYYYY
KR20130067314		CDR1	37-CDR2	37-CDR3	9-CDR1	9-CDR2	9-CDR3	YYYYYY
US20100254975	Eventor	nort CDR1	37-CDR2	37-CDR3	9-CDR1	9-CDR2	9-CDR3	YYYYYY
US20120177662	Excel ex	CDR1	37-CDR2	37-CDR3	9-CDR1	9-CDR2	9-CDR3	YYYYYY
US20120183561	<u>~</u>	CDR1	37-CDR2	37-CDR3	9-CDR1	9-CDR2	9-CDR3	YYYYYY
US20130302354	6	37-CDR1	37-CDR2	37-CDR3	9-CDR1	9-CDR2	9-CDR3	YYYYYY
US20140322209	6	37-CDR1	37-CDR2	37-CDR3	9-CDR1	9-CDR2	9-CDR3	YYYYYY
US20150086563	6	37-CDR1	37-CDR2	37-CDR3	9-CDR1	9-CDR2	9-CDR3	YYYYYY
US20170275365	6	37-CDR1	37-CDR2	37-CDR3	9-CDR1	9-CDR2	9-CDR3	YYYYYY
US8444981	6	37-CDR1	37-CDR2	37-CDR3	9-CDR1	9-CDR2	9-CDR3	YYYYYY
US8454961	6	37-CDR1	37-CDR2	37-CDR3	9-CDR1	9-CDR2	9-CDR3	YYYYYY
US8454962	6	37-CDR1	37-CDR2	37-CDR3	9-CDR1	9-CDR2	9-CDR3	YYYYYY
US8871490	6	37-CDR1	37-CDR2	37-CDR3	9-CDR1	9-CDR2	9-CDR3	YYYYYY
US9499620	6	37-CDR1	37-CDR2	37-CDR3	9-CDR1	9-CDR2	9-CDR3	YYYYYY
WO2010107752	6	37-CDR1	37-CDR2	37-CDR3	9-CDR1	9-CDR2	9-CDR3	YYYYYY
WO2013078375	6	37-CDR1	37-CDR2	37-CDR3	9-CDR1	9-CDR2	9-CDR3	YYYYYY
WO2017180587	6	37-CDR1	37-CDR2	37-CDR3	9-CDR1	9-CDR2	9-CDR3	YYYYYY





#### 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 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.