

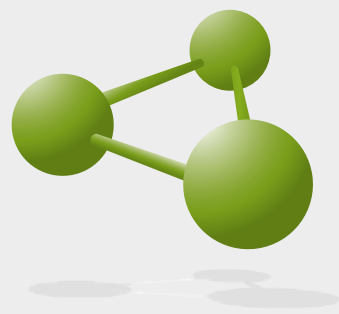
3DM BIO-PRODUCT

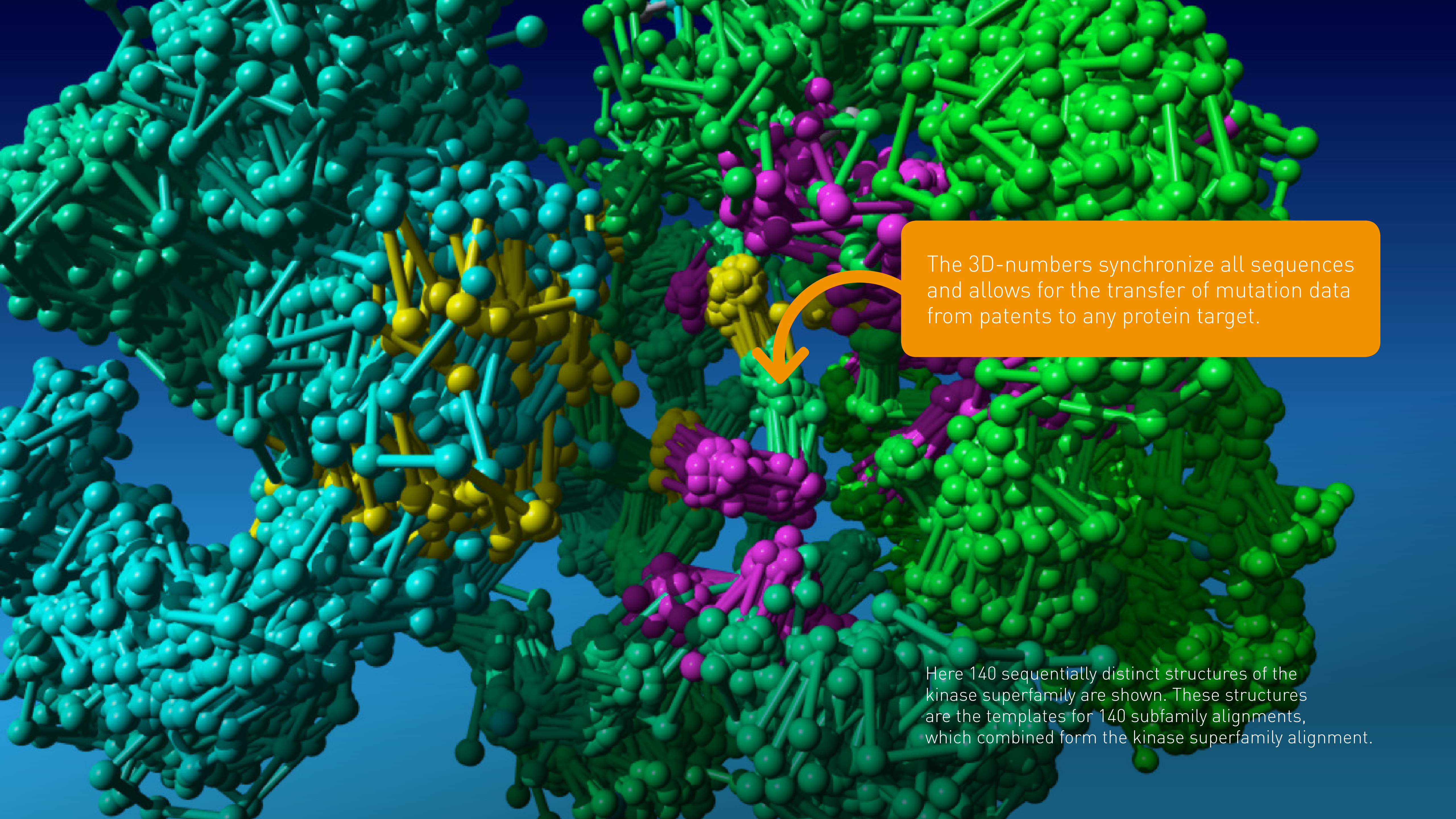
Henk-Jan Joosten

1. 3DM introduction
2. 3DM's patent analysis tool



1. 3DM INTRODUCTION





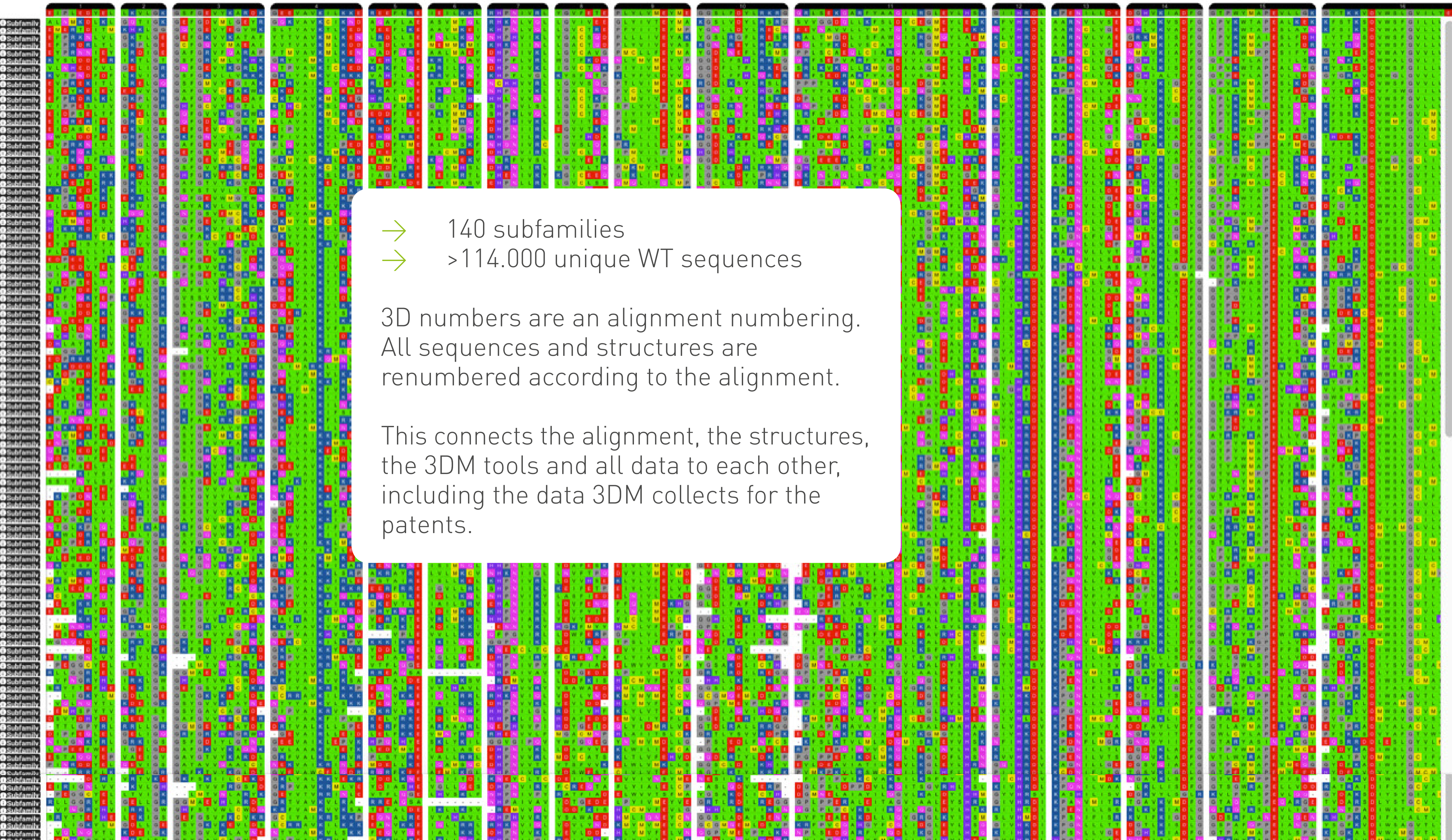
The 3D-numbers synchronize all sequences and allows for the transfer of mutation data from patents to any protein target.

Here 140 sequentially distinct structures of the kinase superfamily are shown. These structures are the templates for 140 subfamily alignments, which combined form the kinase superfamily alignment.



- 3DM System
- Start
- Alignment
- Alignment statistics
- Correlated mutations
- Visualize
- Phylogeny
- Panel design
- Patents
- Search
- System
- 3DM Systems

- 18YGA
- 3KFAA
- 2X2LA
- 3CLYA
- 1L1FA
- 1RDOE
- 3CBLA
- 1O6LA
- 1P4QA
- 2EYAA
- 2X1RA
- 3P6GB
- 3GENA
- 1MP9A
- 2OOLA
- 2VDFB
- 2YFKA
- 3BRBA
- 3C4ZA
- 3EQRA
- 3LXPA
- 3POZA
- 3RCJA
- 2SRCA
- 3AUXB
- 3LXLA
- 3PVJA
- 3V5OB
- 2RKUA
- 1J1BB
- 1XBBA
- 3A7IA
- 3ODIA
- 3KMUA
- 3MIYA
- 3KKBA
- 1PHKA
- 1XJDA
- 2WEIA
- 3BHFA
- 3GZFA
- 3IECA
- 3KVWA
- 2BUJA
- 2J3IA
- 3EGCA
- 3D51A
- 3M9IA
- 1TKJA
- 2EL9A
- 2H6DA
- 3HMMA
- 3LM5A
- 3TKUA
- 4AAUA
- 1U59B
- 2W5AA
- 2X7FA
- 3DTCA
- 3HMFA
- 3ISSF
- 2CLOA
- 3N9XA
- 3OG7B
- 3P65B
- 3QYZA
- 3SOCB
- 2VX3B
- 3ZYAA
- 3Z2WB
- 1FV9B
- 2X4FA
- 2XRIWA
- 2R3IA
- 2W4QA
- 2WQMA
- 3DLSD
- 3EBGC
- 3HKQA
- 3L3TA
- 3RD4A
- 3NSZA
- 2PMLX
- 2R1QA
- 3GNIB
- 3ORKA
- 1WAKA
- 1X8BA
- 2WTKF
- 2ZV2A
- 3PG1A
- 1K0BB
- 2H34B
- 2Y4IB
- 2J2RA
- 2J7TA
- 2WV6B
- 3D4KB
- 3D4MA
- 2PMLX
- 2R1QA
- 3GNIB
- 3ORKA
- 1WAKA
- 1X8BA
- 2WTKF
- 2ZV2A
- 3PG1A



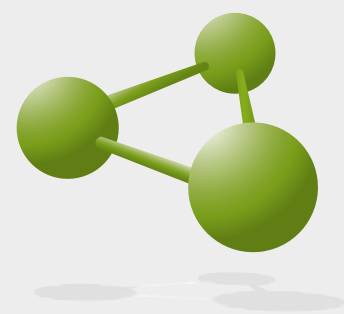
→ 140 subfamilies
 → >114.000 unique WT sequences

3D numbers are an alignment numbering. All sequences and structures are renumbered according to the alignment.

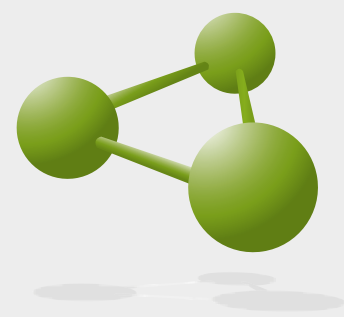
This connects the alignment, the structures, the 3DM tools and all data to each other, including the data 3DM collects for the patents.

MANY DIFFERENT DATA TYPES ARE COLLECTED FOR ALL SEQUENCES IN THESE LARGE ALIGNMENTS

- **Mutation data**
literature, Patents, Swiss-Prot, OMIM, ...
> 264.605 kinase mutations **searchable for effects and transferable to any target protein!**
- **Structure data**
PPI, ligand contacts, bridges, solvent accessibility, flexibility/RMSD, ...
- **Alignment data**
Conservation, correlated mutations, family specific residues, ...
- **SNP data**
SNP databases, genome sequencing projects
- **Data- and tool integration**
All data are stored connected to the 3D numbering scheme and thus to the alignment, to the structures, all 3DM tools, and each other.



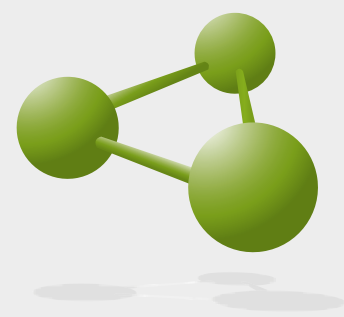
2. 3DM'S PATENT ANALYSIS TOOL



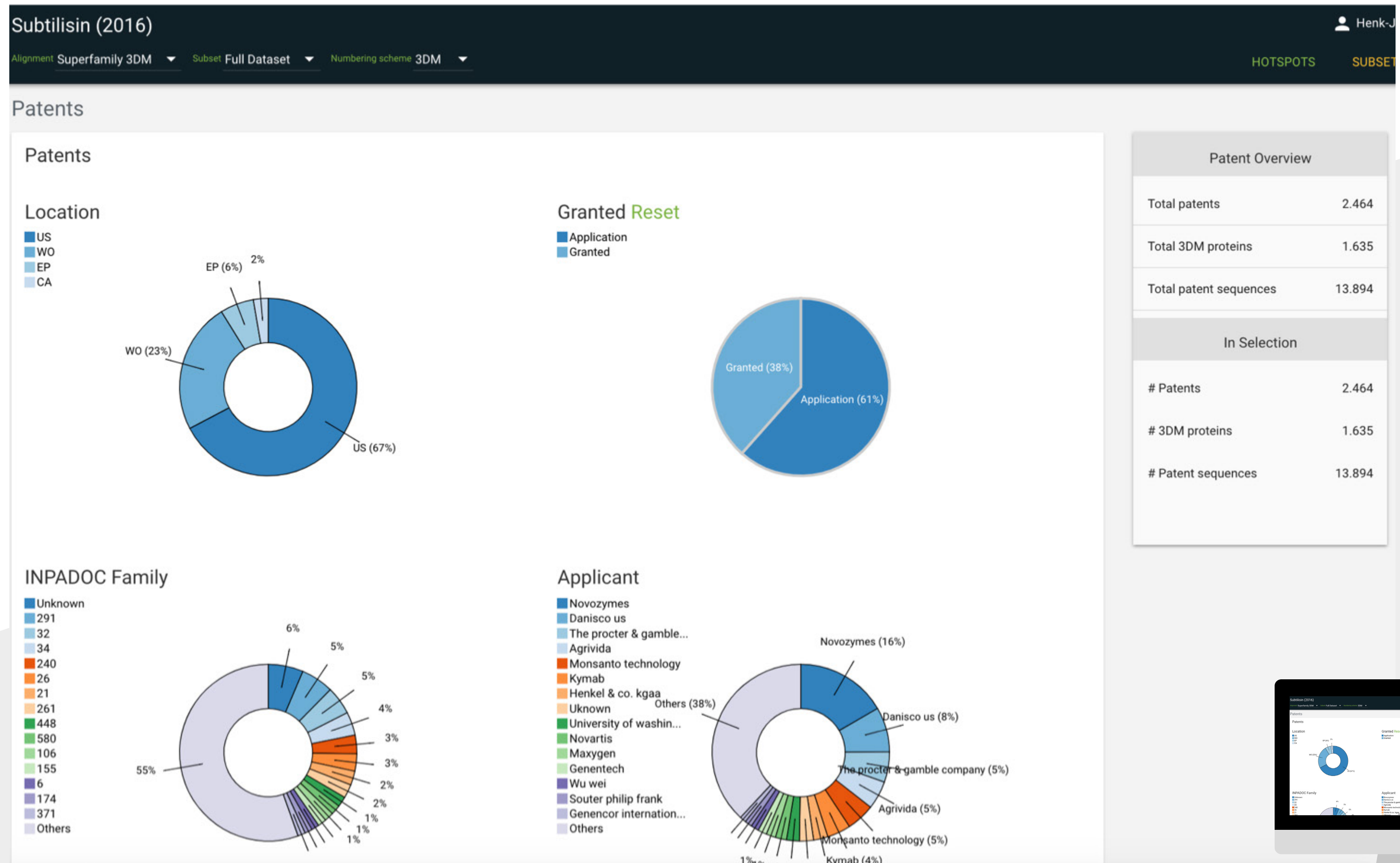
PATENT DATA EXTRACTION

→ **Collection of patents for complete protein families**

- › Claimed sequences
- › Claimed sequence spaces
- › Claimed mutations
- › Publication data
- › Inventors
- › Many other data types



DIFFERENT ONLINE SELECTION TOOLS FOR ANALYSIS OF THE PATENTS

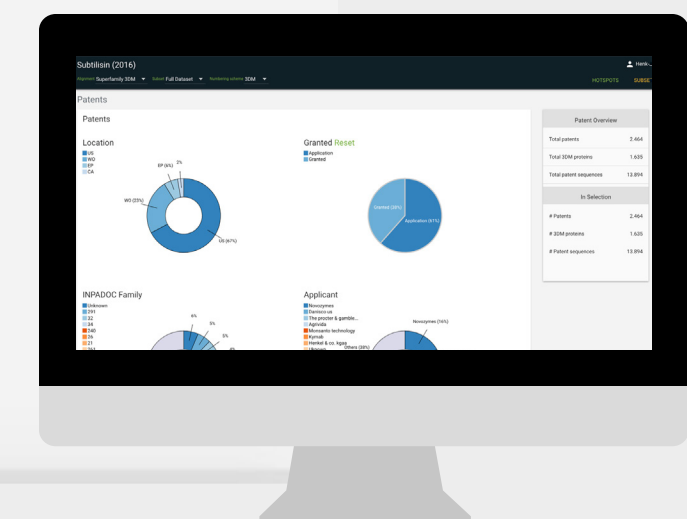
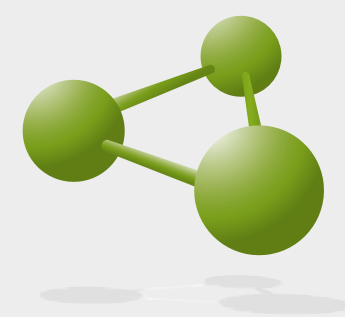


Patent Overview

Total patents	2.464
Total 3DM proteins	1.635
Total patent sequences	13.894

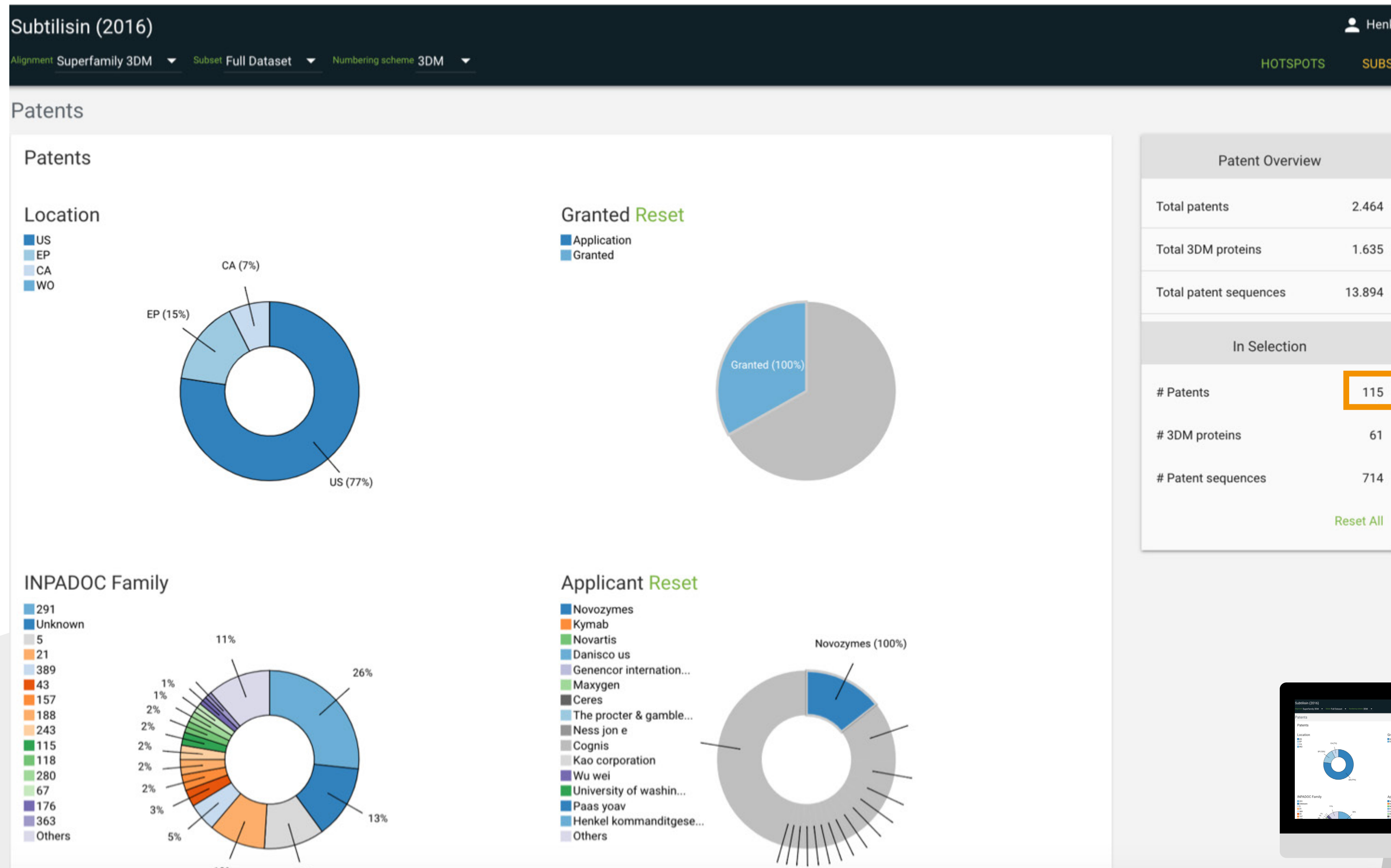
In Selection

# Patents	2.464
# 3DM proteins	1.635
# Patent sequences	13.894

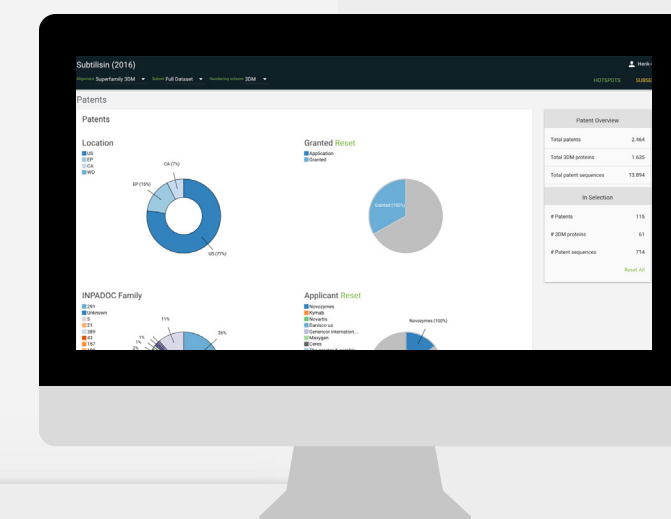
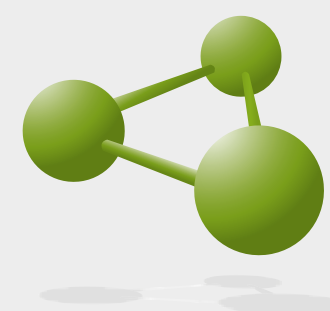


DIFFERENT ONLINE SELECTION TOOLS FOR ANALYSIS OF THE PATENTS

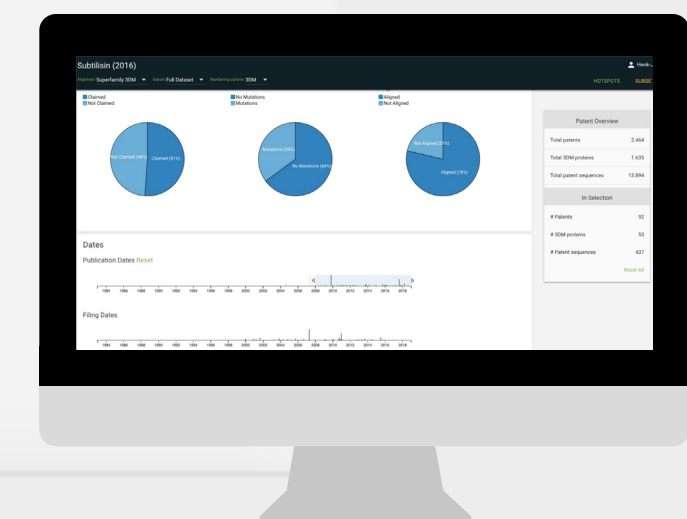
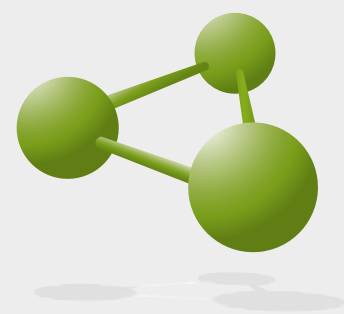
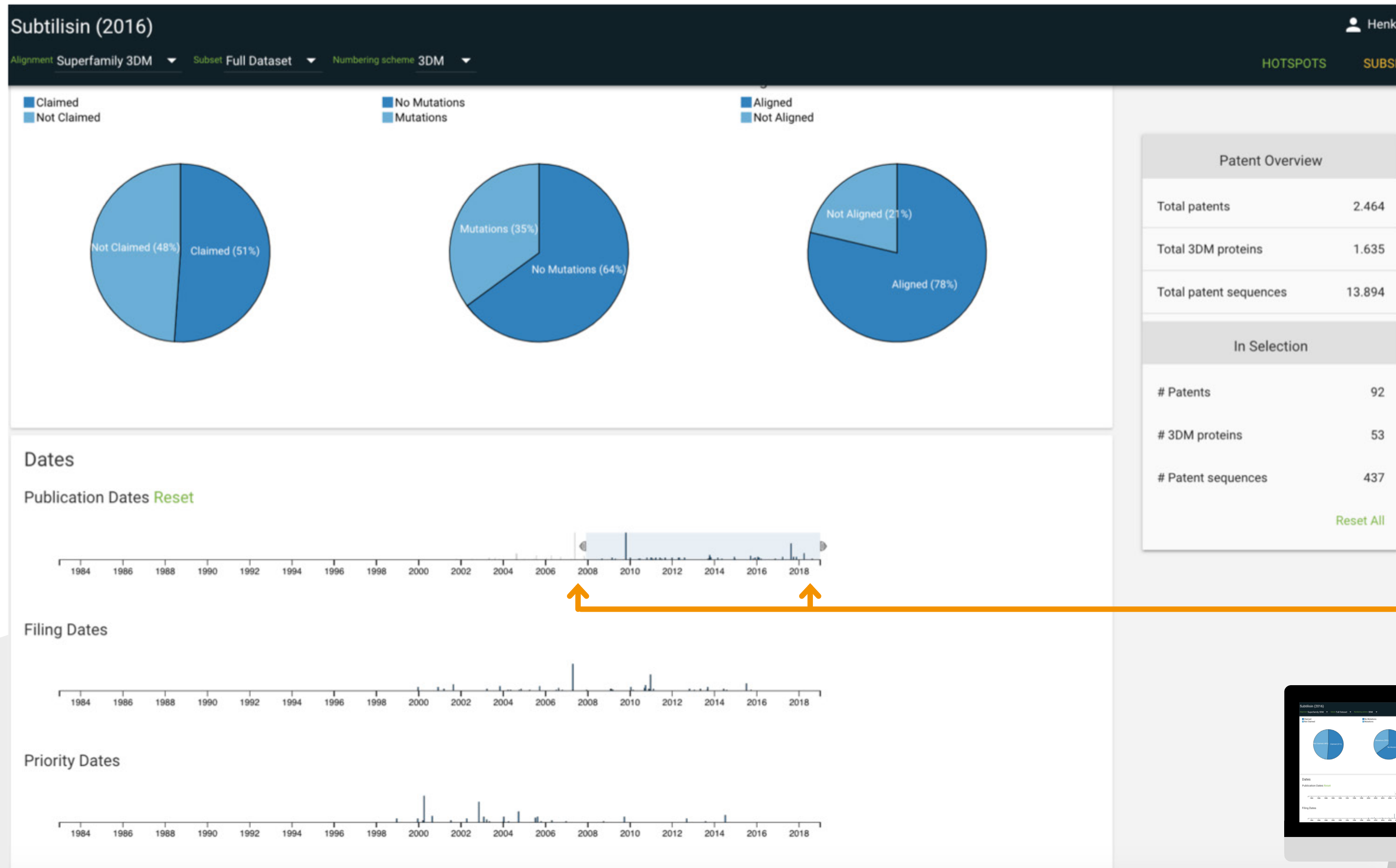
Here all granted patents from Novozymes are selected.



The selection results in 115 patents



DIFFERENT ONLINE SELECTION TOOLS FOR ANALYSIS OF THE PATENTS



DIFFERENT VISUALISATION OPTIONS

Patent sequence mutation positions **i** [Reset](#)

mutations

1 2 3 4 5 6 7 8 9 10 11 12 13 14 15 16 17 18 19 20 21 22 23 24 25 26 27 28 29 30 31 32 33 34 35 36 37 38 39 40 41 42 43 44 45 46 47 48 49 50 51 52 53 54 55 56 57 58 59 60 61 62 63 64 65 66 67 68 69 70 71 72 73 74 75 76 77 78 79 80 81 82 83 84 85 86 87 88 89 90 91 92 93 94 95 96 97 98 99 100 101 102 103

Search

Text search [SEARCH](#) Search patent identifier Search Applicant

[CLEAR](#) [CLEAR](#) [CLEAR](#)

Patents

Export phylogenetic tree [OPEN PHYLOGENETIC TREE](#)

iTol tree options [STEP 1: CREATE CUSTOM ITOL TREE](#)

Patent Overview

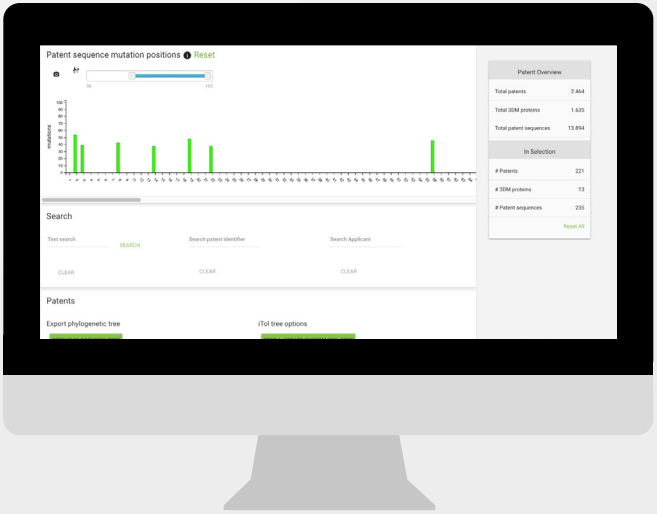
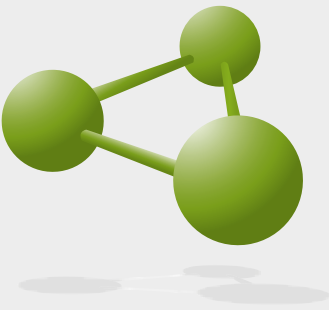
Total patents	2.464
Total 3DM proteins	1.635
Total patent sequences	13.894

In Selection

# Patents	221
# 3DM proteins	13
# Patent sequences	235

[Reset All](#)

Interactive histogram visualising mutations claimed by novozymes.



MANY OPTIONS FOR VISUALIZING PATENT DATA

Patent sequence mutation positions **Reset**

36

mutations

Position	Mutations
1	55
2	40
3	0
4	0
5	0
6	45
7	0
8	0
9	38
10	0
11	48
12	38
13	0
14	0
15	0
16	0
17	0
18	0
19	0
20	0
21	0
22	0
23	0
24	0
25	0
26	0
27	0
28	0
29	0
30	0
31	0
32	0
33	0
34	0
35	0
36	45

Search

Text search **SEARCH**

CLEAR

Patents

Export phylogenetic tree **OPEN PHYLOGENETIC TREE**

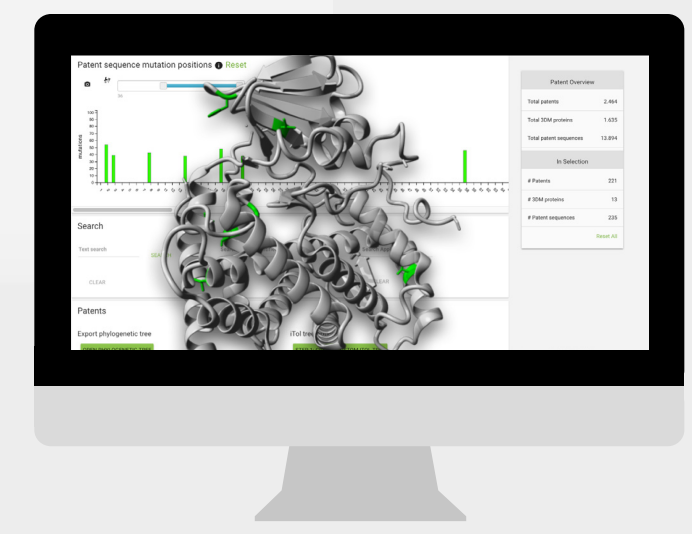
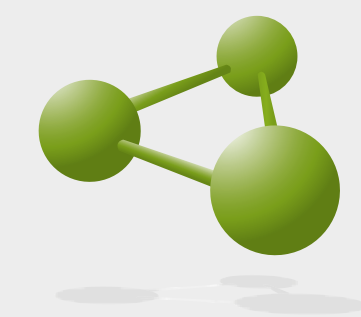
iTol tree **STEP 1: CREATE CUSTOM ITOL TREE**

Patent Overview	
Total patents	2.464
Total 3DM proteins	1.635
Total patent sequences	13.894

In Selection	
# Patents	221
# 3DM proteins	13
# Patent sequences	235

Reset All

The selected mutation data can instantly be visualized in any available protein structure or homolgy model.



MANY OPTIONS FOR VISUALIZING PATENT DATA

The patented sequences can instantly be visualized in the phylogenetic tree of the superfamily for FTO analysis.

Patent sequence mutation p

36

mutations

100
90
80
70
60
50
40
30
20
10
0

1 2 3 4 5 6 7 8 9 10 11 12 13

Search

Text search

Patents

Export phylogenetic tree

Save/resto

view

2.464

1.635

s 13.894

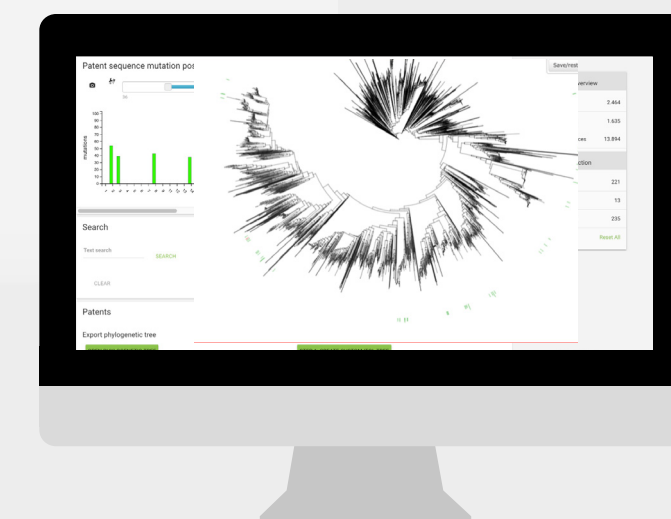
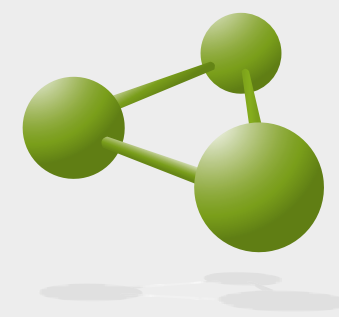
ion

221

13

235

STEP 1: CREATE CUSTOM ITOL TREE



SUMMARY OF THE SELECTED PATENTS IS PROVIDED

Link to interactive analysis tool for each patent

Patent List

[DOWNLOAD PATENT SEQUENCES](#)

First Previous **1** 2 Next Last

92 patents in selection

[Family:115 - US7951573 B2](#) [External link](#)

Subtilases

Applicant: Novozymes Publication type: Granted Sequences: 8

Published: 31/05/2011
Filed: 18/11/2010
Priority: 16/08/2005

Abstract

The present invention relates to novel subtilases from wild-type strains of Bacillus, especially the Bacillus strains ZI344, EP655, P203, EP63, ZI120, ZI130, ZI1342 and ZI140, and to methods of construction and production of these proteases. Further, the present invention relates to use of the claimed subtilases in detergents, such as a laundry detergent or an automatic dishwashing detergent.

Patented sequences [Show more...](#)

SEQ ID	Claimed	Mutations	Linked protein in 3DM	Similarity	Claimed seq. space
2	Not Claimed	0	S5VEF0	81.87%	
4	Not Claimed	0	S5VEF0	82.93%	
6	Not Claimed	0	S5VEF0	82.93%	

A list of the selected patents is provided.

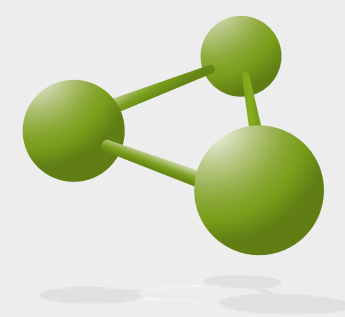
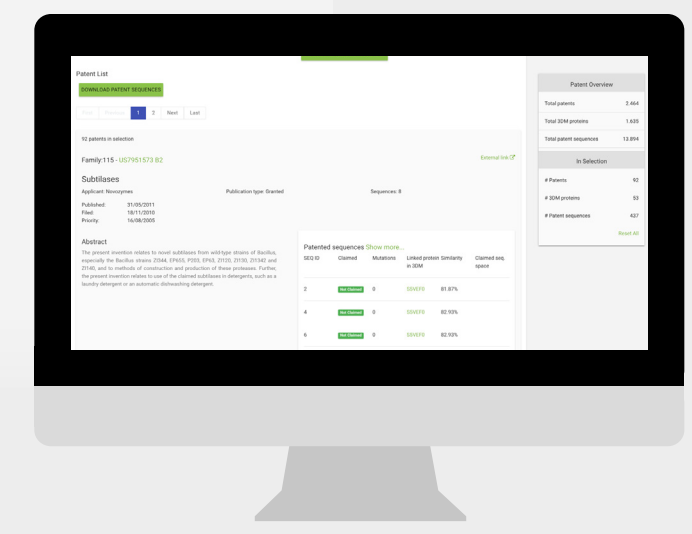
Patent Overview

Total patents	2.464
Total 3DM proteins	1.635
Total patent sequences	13.894

In Selection

# Patents	92
# 3DM proteins	53
# Patent sequences	437

[Reset All](#)



INTERACTIVE TOOL FOR ANALYSIS A PATENT SHOWING CLAIMED SEQUENCES AND MUTATIONS

Subtilisin (2016)
Henk-Jan Joosten

Alignment Superfamily 3DM Subset Full Dataset Numbering scheme 3DM
HOTSPOTS SUBSETS

patent US9133423 B2

SUBTILASE VARIANTS

Applicant: NOVOZYMES A/S, [External link](#)

Abstract

The present invention relates to novel subtilase variants exhibiting improvements relative to the parent subtilase in one or more properties including: wash performance, thermal stability, storage stability or catalytic activity. The variants of the invention are suitable for use in e.g., cleaning or detergent compositions, such as laundry detergent compositions and dish wash compositions, including automatic dish wash compositions.

Type: Granted
Published: 15/09/2015
Filed: 15/01/2010
Priority: 08/07/2005

Simple family members

[US20100120091 A1](#)

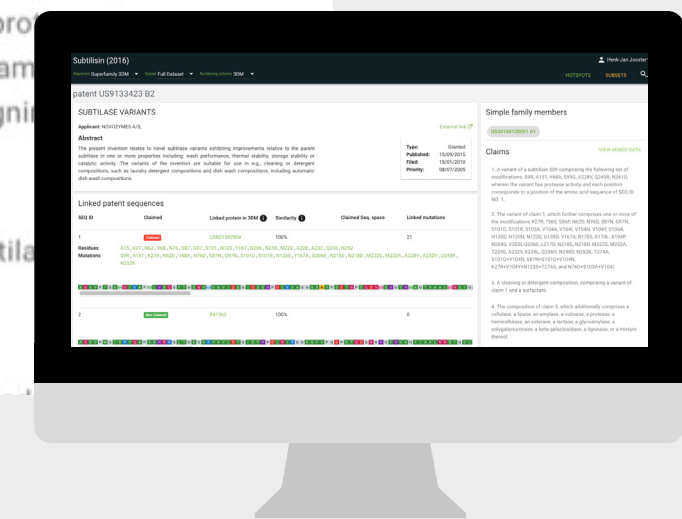
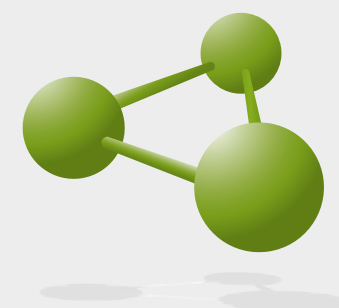
Claims

[VIEW MINED DATA](#)

1. A variant of a subtilisin 309 comprising the following set of modifications: S9R, A15T, V68A, S99G, A228V, Q245R, N261D; wherein the variant has protease activity and each position corresponds to a position of the amino acid sequence of SEQ ID NO: 1.
2. The variant of claim 1, which further comprises one or more of the modifications K27R, *36D, S56P, N62D, N76D, S87N, G97N, S101G, S101R, S103A, V104A, V104I, V104N, V104Y, S106A, H120D, H120N, N123S, G159D, Y167A, R170S, R170L, A194P, N204D, V205I, Q206E, L217D, N218S, N218D, M222S, M222A, T224S, A232V, K235L, Q236H, N248D, N252K, T274A, S101G+V104N, S87N+S101G+V104N, K27R+V104Y+N123S+T274A, and N76D+S103A+V104I.
3. A cleaning or detergent composition, comprising a variant of claim 1 and a surfactant.
4. The composition of claim 3, which additionally comprises a cellulase, a lipase, an amylase, a cutinase, a protease, a hemicellulase, an esterase, a lactase, a glycoamylase, a polygalacturonase, a beta-galactosidase, a ligninase, or any thereof.
5. An isolated DNA sequence encoding a subtilase variant of claim 1.

Linked patent sequences

SEQ ID	Claimed	Linked protein in 3DM	Similarity	Claimed Seq. space	Linked mutations
1	Claimed	LDN21592904	100%		21
Residues	A15, K27, N62, V68, N76, S87, G97, S101, N123, Y167, Q206, N218, M222, A228, A232, Q245, N252				
Mutations	S9R, A15T, K27R, N62D, V68A, N76D, S87N, G97N, S101G, S101R, N123S, Y167A, Q206E, N218S, N218D, M222S, M222A, A228V, A232V, Q245R, N252K				
<div style="font-family: monospace; font-size: 0.8em; color: #2c3e50;"> A Q S V P Y G V S Q I K A P A L H S Q G Y T G S N V K V A V I D S G I D S S H P D L K V A G G A S M V P S E T N P F O D N K S H G T H V A G T V A A L N S I G </div>					
2	Not Claimed	P41362	100%		0
<div style="font-family: monospace; font-size: 0.8em; color: #2c3e50;"> A Q S V P W G I S R V Q A P A A H N R G L T G S G V K V A V L D T G I S T H P D L N I R G G A S F V P G E P S T Q D G N G H G T H V A G T I A A L N N S I G V L </div>					



MOVING MOUSE OVER DATA WILL HIGHLIGHT THE CLAIM IN WHICH 3DM FOUND THE SELECTED DATA POINT

Subtilisin (2016) Henk-Jan Joosten

Alignment Superfamily 3DM Subset Full Dataset Numbering scheme 3DM HOTSPOTS SUBSETS

patent US9133423 B2

SUBTILASE VARIANTS

Applicant: NOVOZYMES A/S. External link

Abstract
 The present invention relates to novel subtilase variants exhibiting improvements relative to the parent subtilase in one or more properties including: wash performance, thermal stability, storage stability or catalytic activity. The variants of the invention are suitable for use in e.g., cleaning or detergent compositions, such as laundry detergent compositions and dish wash compositions, including automatic dish wash compositions.

Type: Granted
Published: 15/09/2015
Filed: 15/01/2010
Priority: 08/07/2005

Simple family members

US20100120091 A1 VIEW MINED DATA

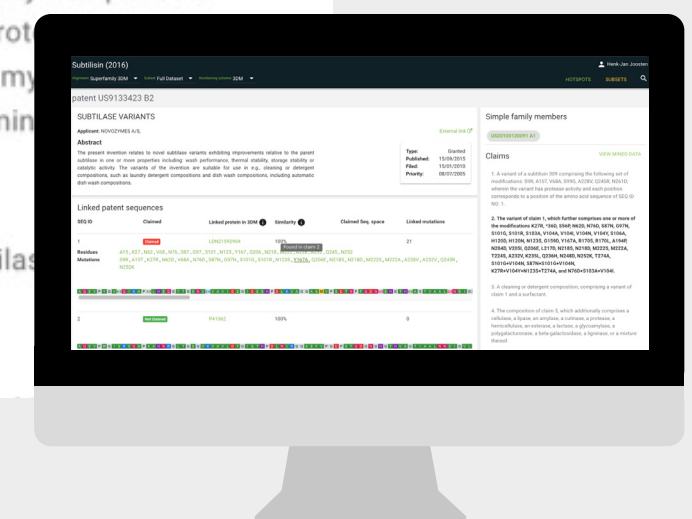
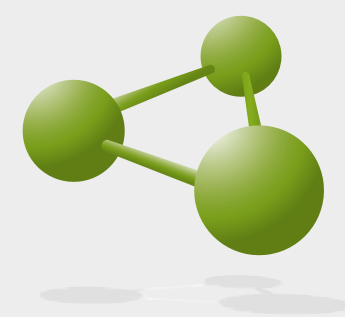
Claims

1. A variant of a subtilisin 309 comprising the following set of modifications: S9R, A15T, V68A, S99G, A228V, Q245R, N261D; wherein the variant has protease activity and each position corresponds to a position of the amino acid sequence of SEQ ID NO: 1.
- 2. The variant of claim 1, which further comprises one or more of the modifications K27R, *36D, S56P, N62D, N76D, S87N, G97N, S101G, S101R, S103A, V104A, V104I, V104N, V104Y, S106A, H120D, H120N, N123S, G159D, Y167A, R170S, R170L, A194P, N204D, V205I, Q206E, L217D, N218S, N218D, M222S, M222A, T224S, A232V, K235L, Q236H, N248D, N252K, T274A, S101G+V104N, S87N+S101G+V104N, K27R+V104Y+N123S+T274A, and N76D+S103A+V104I.**
3. A cleaning or detergent composition, comprising a variant of claim 1 and a surfactant.
4. The composition of claim 3, which additionally comprises a cellulase, a lipase, an amylase, a cutinase, a protease, a hemicellulase, an esterase, a lactase, a glycoamylase, a polygalacturonase, a beta-galactosidase, a ligninase or any combination thereof.
5. An isolated DNA sequence encoding a subtilase variant of claim 1.

Linked patent sequences

SEQ ID	Claimed	Linked protein in 3DM	Similarity	Claimed Seq. space	Linked mutations
1	Claimed	LDN21592904	100% <small>Found in claim 2</small>		21
<p>Residues A15, K27, N62, V68, N76, S87, G97, S101, N123, Y167, Q206, N218, M222, A228, A232, Q245, N252</p> <p>Mutations S9R, A15T, K27R, N62D, V68A, N76D, S87N, G97N, S101G, S101R, N123S, <u>Y167A</u>, K205E, N218S, N218D, M222S, M222A, T224S, A232V, K235L, Q236H, N248D, N252K, T274A, N252K</p> <p>A Q S V P Y G V I S Q I K A P A L H S Q G Y T G S N V K V A V I D S G I D S S H P D L K V A G G A S M V P S E T N P F Q D N N S H G T H V A G T V A A L N N S I G</p>					
2	Not Claimed	P41362	100%		0
<p>A Q S V P W G I S R V Q A P A A H N R G L T G S G V K V A V L D T G I S T H P D L N I R G G A S F V P G E P S T O D G N G H G T H V A G T I A A L N N S I G V L</p>					

Mouse over on mutations highlights the claim



TOOL FOR PROJECTING PATENT DATA ON A CUSTOM TARGET SEQUENCE

GENERAL SEQUENCE SEQUENCE PROJECTION (BETA)

Sequence

QQTVPWGITRVQAPAVHNRGITGSGVRVAILDGISAHSDLNIRGGASFVPGEPTTADLNHGHGTHVAGTVAALNNSIGV I 80
GVAPNAELYAVKVLGANGSGSVSGIAQGLEWAATNNMHIANMSLGSDFPSSTLERAVNYATSRDVLVIAATGNNGSGSVG 160
YPARYANAMAVGATDQNNRRANFSQYGTGIDIVAPGVNVQSTYPGNRYVSMNGTSMATPHVAGAAALVKQRYPSWNATQ I 240
RNHLKNTATNLGNSSQFGSLVNAEAATR

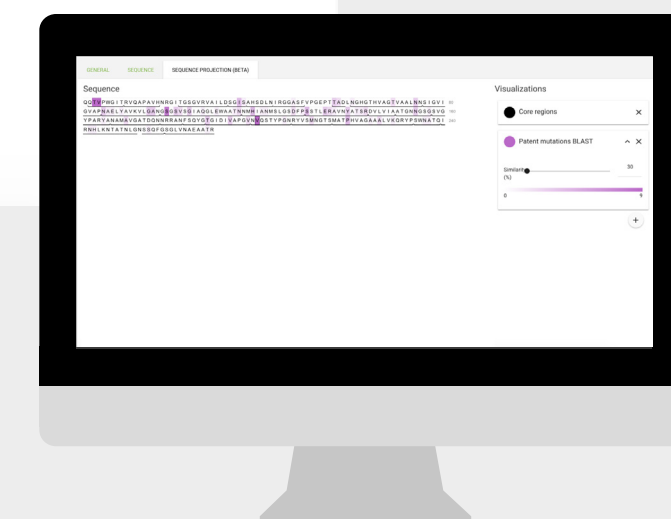
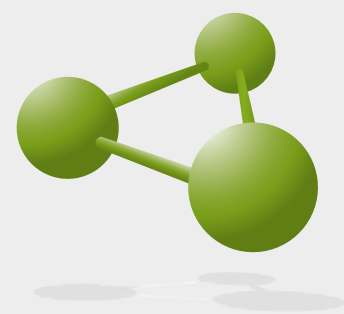
Visualizations

- Core regions
- Patent mutations BLAST

Similarity (%) 30

1. Custom sequences can be uploaded to 3DM
2. 3DM connects the sequence to the alignment
3. Blast searches can be performed against the patented sequences
4. Patented mutations are visualized in the target sequence (purple residues)

Here the cut-off was set on 30% sequence identity. So, all mutations claimed in sequences that are >30% identical are plotted on the target sequence.



CLICKING ON A PURPLE RESIDUE PROVIDES A LIST OF PATENTS THAT HAVE CLAIMED MUTATIONS AT THE SELECTED POSITION

GENERAL SEQUENCE SEQUENCE PROJECTION (BETA)

Sequence

QQTVPWGI TRVQAPAVHNRGI TGSGVRVA ILDSGI SAHSDLNIRGGASFVPGEPTTADLNHGHGTHVAGTVAALNNSIGVI 80
GVAPNAELYAVKVLGANGSGSVSGIAQGLEWAATNNMHI ANMSLGSDFPSSTLERAVNYATSRDVLVIAATGNNGSGSVG 160
YPARYANAMAVGATDQNNRRANFSQYGTGIDIVAPGVNVQSTYPGNRYVSMNGTSMATPHVAGAAALVKQRYPSWNATQI 240
RNHLKNTATNLGNSSQFGSGLVNAEAATR

V 199 Valine (Val)
Alignment position: 191 (aligned in core region)

STORAGE-STABLE LIQUID DISHWASHING DETERGENT CONTAINING PROTEASE AND AMYLASE **2 Patents in simple family**

In a liquid dishwashing detergent comprising a protease and amylase, storage stability is to be improved. This is achieved through the use of a protease comprising an amino acid sequence having at least 70% identity over its total length with the amino acid sequence specified in SEQ ID NO. 1 and having, in the listing according to SEQ ID NO. 1, the L211D amino acid substitution in combination with at least two further amino acid substitutions selected from the group consisting of S3T, V4I, V193M and V199I.

Mutations

SEQ ID NO:1 Similarity: 91% V199I V

SEQ ID NO:1 Similarity: 91% V199I V

Abstract differs

US20150017707 A1
Publication: 2015-01-15
Applicant: BASF SE

EP2809763 B1 **Granted**
Publication: 2017-01-04
Applicant: BASF SE

Patent family members without mutations at this position: WO2013113619 A1

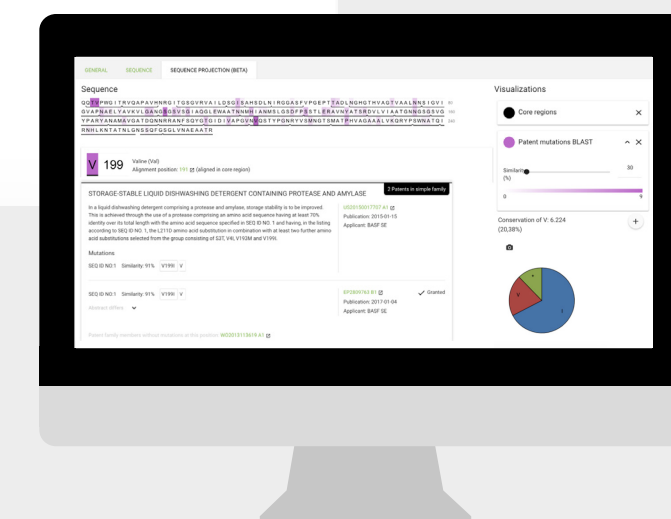
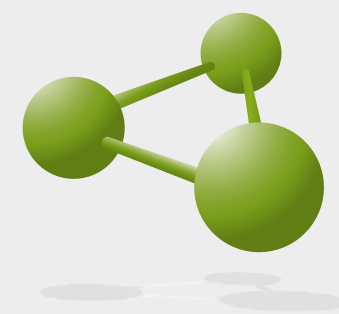
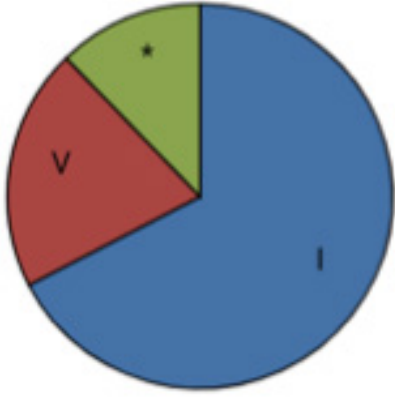
Visualizations

Core regions

Patent mutations BLAST

Similarity (%) 30

Conservation of V: 6.224 (20,38%)



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