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(54) **DEVICE FOR PRESENTING SEQUENCING DATA**

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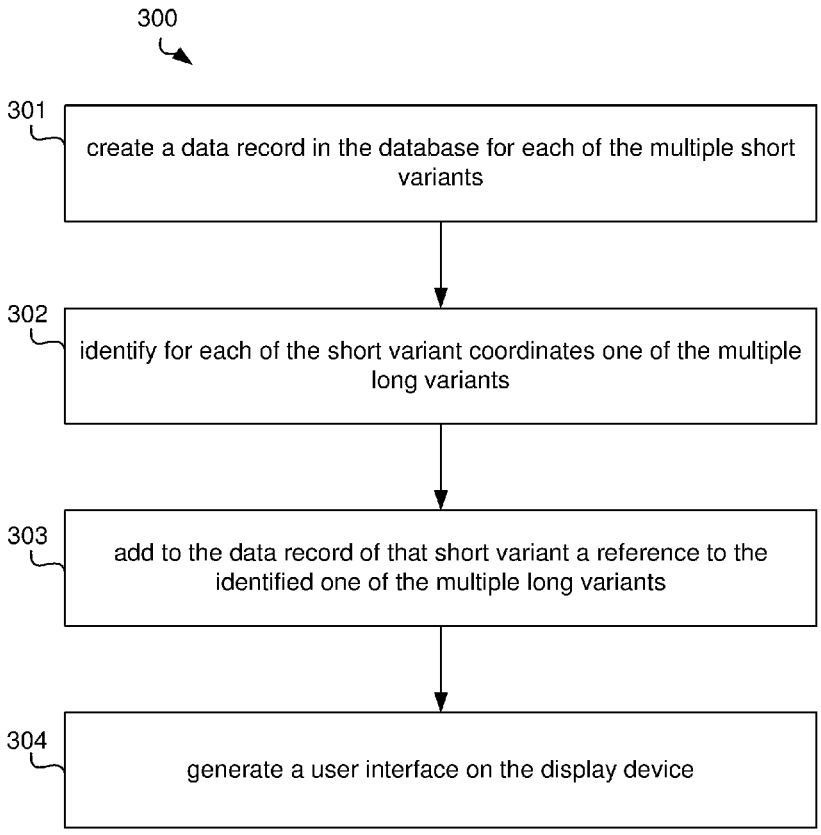
(57) **ABSTRACT**

This disclosure relates to a device for presenting whole genome sequence data. A file system stores a first file comprising short variant data and a second file comprising long variant data. A database stores variant data as data records. A display device displays a representation of variants. Finally, a processor is configured to create a data record in the database for each of the multiple short variants and identify for each of the short variant coordinates one of the multiple long variants. The processor then adds to the data record of that short variant a reference to the identified one of the multiple long variants. The processor also generates a user interface with a representation of the multiple short variants that comprise long variant data of the long variant according to the reference from the data record for each of the multiple short variants.



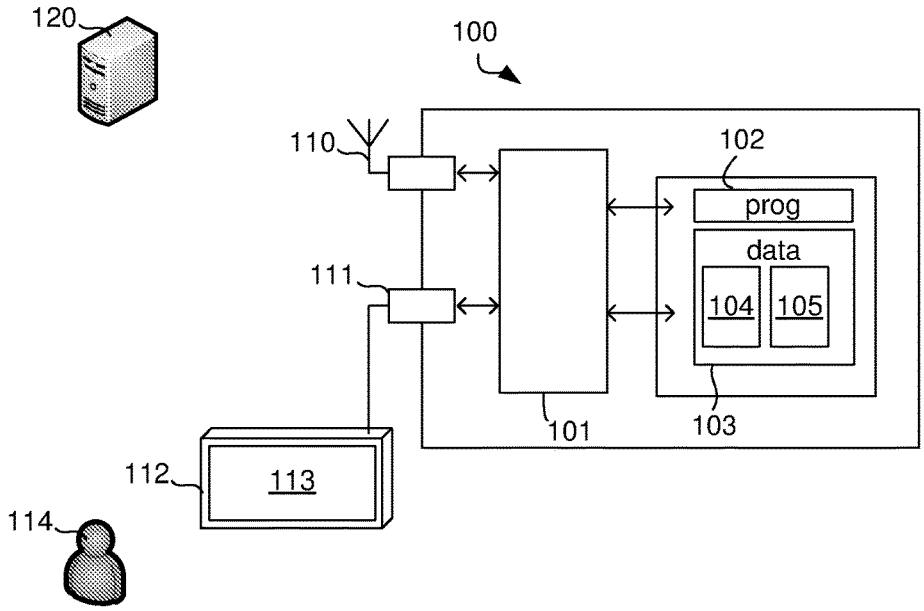

120
100
110
102
prog
data
111
104
105
101
103
112
113
114

Fig. 1

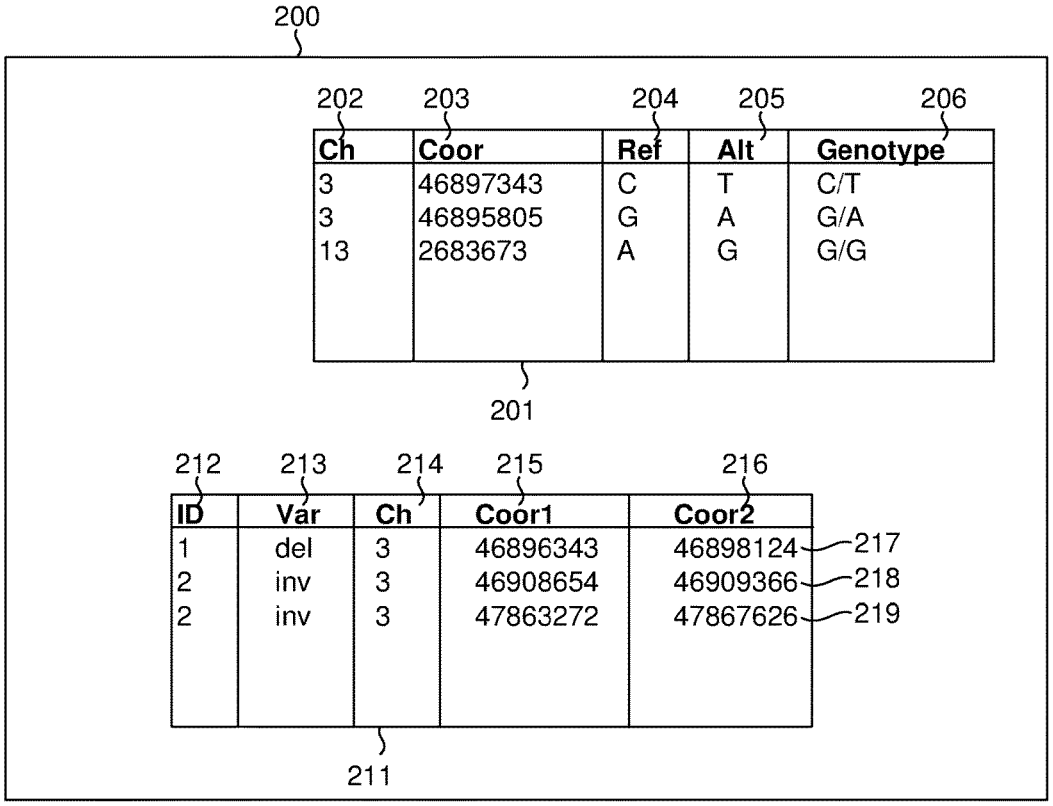

200
202
203
204
205
206
Ch
Coor
Ref
Alt
Genotype
3
46897343
C
T
C/T
3
46895805
G
A
G/A
13
2683673
A
G
G/G
201
212
213
214
215
216
ID
Var
Ch
Coor1
Coor2
1
del
3
46896343
46898124
217
2
inv
3
46908654
46909366
218
2
inv
3
47863272
47867626
219
211

Fig. 2

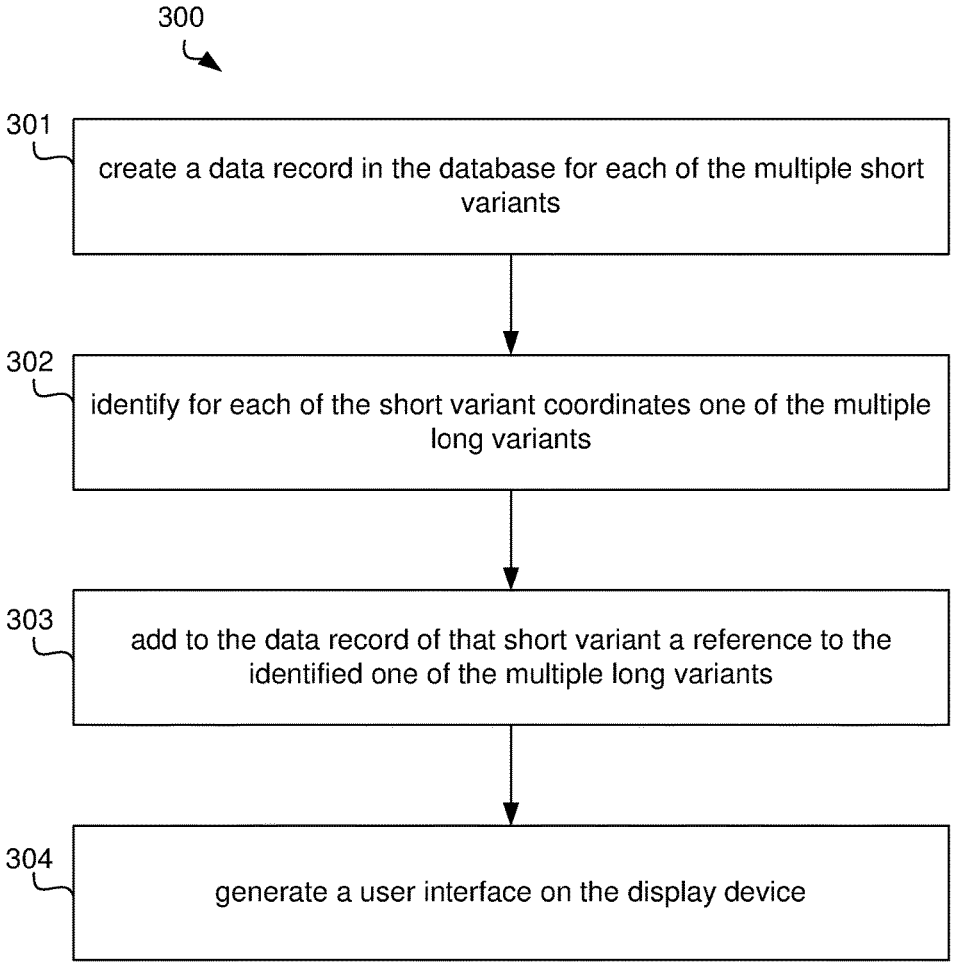

300
301
create a data record in the database for each of the multiple short variants
302
identify for each of the short variant coordinates one of the multiple long variants
303
add to the data record of that short variant a reference to the identified one of the multiple long variants
304
generate a user interface on the display device

Fig. 3

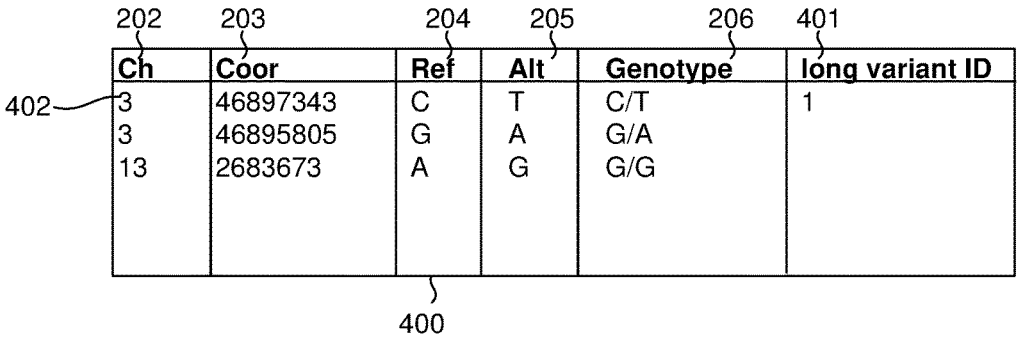

202
203
204
205
206
401
Ch
Coor
Ref
Alt
Genotype
long variant ID
402
3
46897343
C
T
C/T
1
3
46895805
G
A
G/A
13
2683673
A
G
G/G
400

Fig. 4

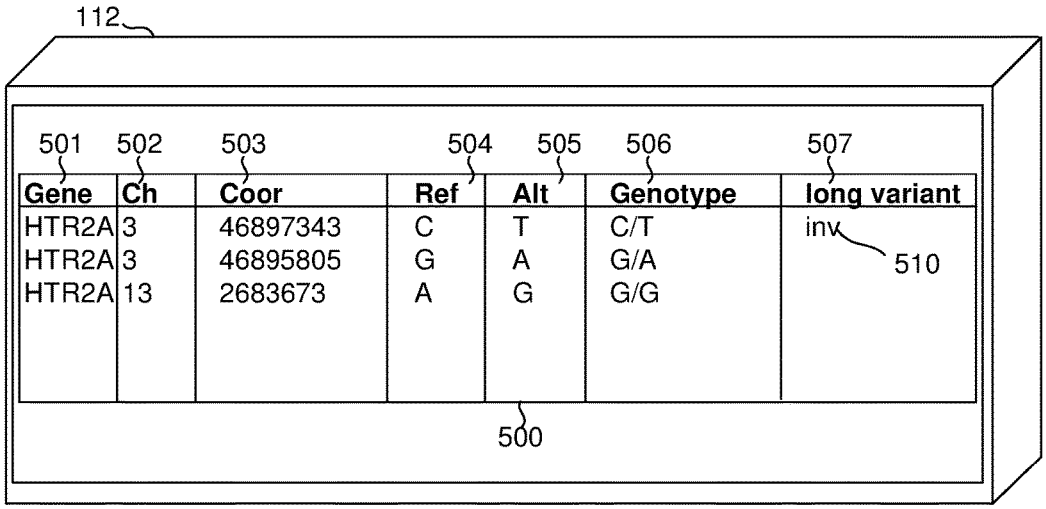

112
501
502
503
504
505
506
507
Gene
Ch
Coor
Ref
Alt
Genotype
long variant
HTR2A
3
46897343
C
T
C/T
inv
HTR2A
3
46895805
G
A
G/A
510
HTR2A
13
2683673
A
G
G/G
500

Fig. 5

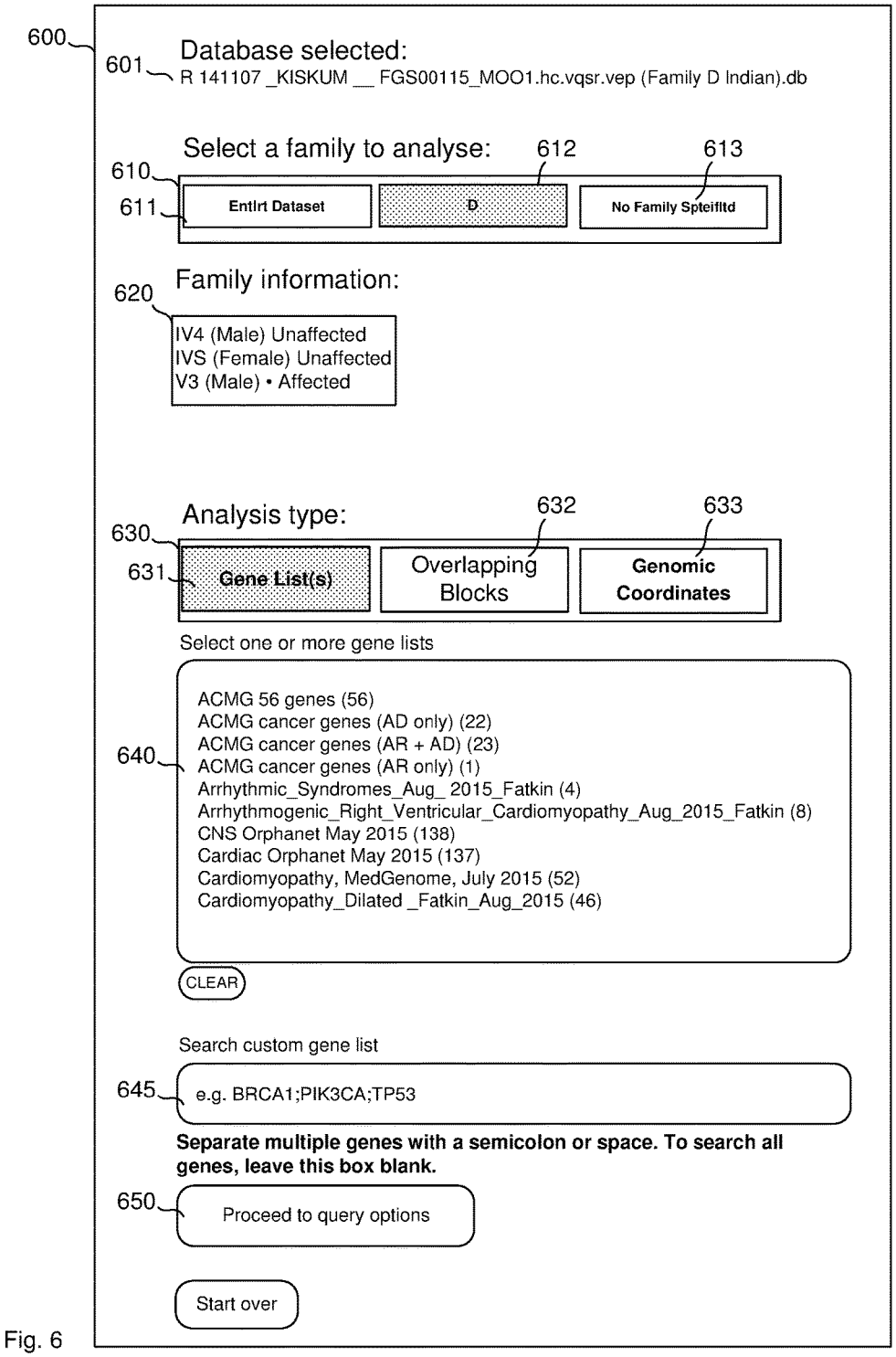

600
601
Database selected:
R 141107 _KISKUM __ FGS00115_MOO1.hc.vqsr.vep (Family D Indian).db
Select a family to analyse:
612
613
610
611
Entlrt Dataset
D
No Family Spteifltd
Family information:
620
IV4 (Male) Unaffected
IVS (Female) Unaffected
V3 (Male) • Affected
Analysis type:
632
633
630
631
Gene List(s)
Overlapping Blocks
Genomic Coordinates
Select one or more gene lists
640
ACMG 56 genes (56)
ACMG cancer genes (AD only) (22)
ACMG cancer genes (AR + AD) (23)
ACMG cancer genes (AR only) (1)
Arrhythmic_Syndromes_Aug_ 2015_Fatkin (4)
Arrhythmogenic_Right_Ventricular_Cardiomyopathy_Aug_2015_Fatkin (8)
CNS Orphanet May 2015 (138)
Cardiac Orphanet May 2015 (137)
Cardiomyopathy, MedGenome, July 2015 (52)
Cardiomyopathy_Dilated _Fatkin_Aug_2015 (46)
CLEAR
Search custom gene list
645
e.g. BRCA1;PIK3CA;TP53
Separate multiple genes with a semicolon or space. To search all genes, leave this box blank.
650
Proceed to query options
Start over

Fig. 6

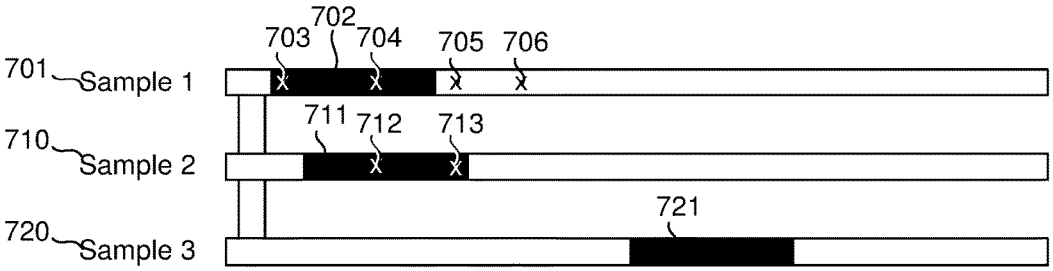

701
Sample 1
703
702
704
705
706
710
Sample 2
711
712
713
720
Sample 3
721

Fig. 7

DEVICE FOR PRESENTING SEQUENCING DATA

CROSS-REFERENCE TO RELATED APPLICATIONS

[0001] The present application claims priority from Australian Provisional Patent Application No 2016903841 filed on 22 Sep. 2016, the content of which is incorporated herein by reference.

TECHNICAL FIELD

[0002] This disclosure relates to devices, methods and systems for presenting whole genome sequence data.

BACKGROUND

[0003] Genetic testing allows the identification of genetic variants, including mutations, that have an effect on the occurrence of a particular disease or phenotype. In particular, specific loci are known to be associated with particular diseases. For example, the BRCA1 gene is known to be associated with breast cancer and a genetic test is available for this particular locus to assist with predicting a likelihood of developing breast cancer.

[0004] Instead of testing at particular loci it is also possible to sequence the entire genome of an individual, which is referred to as Whole Genome Sequencing (WGS). WGS provides more detailed insight into a person's genome than testing at specific loci and allows a more personalised diagnosis or prognosis. However, it is difficult for clinicians, researchers and other users to manually review the large data sets created by WGS. In particular, for professionals who have a practical knowledge of the genome instead of research knowledge it is difficult to use WGS data efficiently in diagnosis or for prognosis.

[0005] Any discussion of documents, acts, materials, devices, articles or the like which has been included in the present specification is not to be taken as an admission that any or all of these matters form part of the prior art base or were common general knowledge in the field relevant to the present disclosure as it existed before the priority date of each claim of this application.

[0006] Throughout this specification the word "comprise", or variations such as "comprises" or "comprising", will be understood to imply the inclusion of a stated element, integer or step, or group of elements, integers or steps, but not the exclusion of any other element, integer or step, or group of elements, integers or steps.

SUMMARY

[0007] A device for presenting whole genome sequence data of a patient comprises:

[0008] a file system to store the whole genome sequence data of the patient, the whole genome sequence data comprising:

[0009] a first data file comprising short variant data related to multiple short variants in the patient at respective short variant coordinates;

[0010] a second data file comprising long variant data related to multiple long variants in the patient at respective long variant coordinates;

[0011] a database to store variant data as data records;

[0012] a display device to display a representation of variants; and

[0013] a processor configured to

[0014] create a data record in the database for each of the multiple short variants,

[0015] identify for each of the short variant coordinates one of the multiple long variants where that short variant coordinate lies within the coordinates of the one of the multiple long variants,

[0016] add to the data record of that short variant a reference to the identified one of the multiple long variants, and

[0017] generate a user interface on the display device, the user interface comprising a representation of the multiple short variants, wherein the representation of the multiple short variants comprises long variant data of the long variant according to the reference from the data record for each of the multiple short variants.

[0018] It is an advantage that a clinical practitioner can view the user interface and can see the multiple short variants together with the references to the long variants. This provides a more useful tool to the practitioner as it allows the combination of two separate data sources into a single view. This way, the practitioner can more efficiently peruse the genomic variations and provide a diagnosis more accurately.

[0019] The processor may be further configured to execute a short variant calling tool to generate the first data file and a long variant calling tool to generate the second data file.

[0020] The long variant calling tool may generate annotation data for each long variant and the reference to the long variant comprises the annotation data.

[0021] The processor may be further configured to:

[0022] repeat the step of executing a long variant calling tool for multiple different long variant calling tools to generate multiple second data files; and

[0023] repeat the steps of identifying one of the multiple long variants and adding to the data record for each of the multiple second data files.

[0024] The reference to the long variant may comprise a concatenation of the annotation data from the multiple long variant calling tools.

[0025] The database may comprise a long variant table to store long variants from the multiple long variant calling tools as separate rows.

[0026] The processor may be further configured to:

[0027] identify an inversion in the whole genome sequence data based on the long variant data; and

[0028] create two data records in the database to represent the inversion.

[0029] The processor may be further configured to:

[0030] identify a translocation in the whole genome sequence data based on the long variant data; and

[0031] create two data records in the database to represent the translocation.

[0032] Creating two data records may comprise creating a link between the two data records.

[0033] The database may be a relational database comprising a table to store links between the two data records.

[0034] The database may comprise a short variant table to store short variants and a long variant table to store long variants and a sample identifier of the whole genome sequence data serves as a common key between the short variant table and the long variant table.

[0035] The database may comprise a gene table to store gene information, wherein the gene information comprises a gene identifier and gene coordinates.

[0036] The short variant table may comprise short variant coordinates and the long variant table comprises long variant coordinates and the short variant coordinates, long variant coordinates and gene coordinates serve as a comment key between the short variant table, the long variant table and the gene table.

[0037] The processor may be further configured to filter the short variant data based on the long variant data.

[0038] The processor may be further configured to filter the short variant data based on an overlap between long variants of different samples and/or long variant calling tools.

[0039] The processor may be further configured to filter the short variant data based on Mendelian inheritance associated with the genomic data.

[0040] The processor may be further configured to filter the short variant data based on copy number data associated with the long variant data.

[0041] A method for presenting whole genome sequence data of an individual comprises:

[0042] receiving the whole genome sequence data of the individual, the whole genome sequence data comprising:

[0043] short variant data related to multiple short variants of the individual at respective short variant coordinates; and

[0044] long variant data related to multiple long variants of the individual at respective long variant coordinates;

[0045] identifying for each of the short variant coordinates one of the multiple long variants where that short variant coordinate lies within the coordinates of the one of the multiple long variants;

[0046] creating an association between that short variant and the identified one of the multiple long variants; and

[0047] generating user interface data, the user interface data comprising a representation of each of the multiple short variants, wherein the representation of each of the multiple short variants comprises long variant data of the identified long variant associated with that short variant.

[0048] Software, when installed on a computer, causes the computer to perform the above method.

[0049] A computer system for presenting whole genome sequence data of an individual comprises:

[0050] a data port to receive the whole genome sequence data of the individual, the whole genome sequence data comprising:

[0051] short variant data related to multiple short variants of the individual at respective short variant coordinates; and

[0052] long variant data related to multiple long variants of the individual at respective long variant coordinates; and

[0053] a processor to:

[0054] identify for each of the short variant coordinates one of the multiple long variants where that short variant coordinate lies within the coordinates of the one of the multiple long variants;

[0055] create an association between that short variant and the identified one of the multiple long variants; and

[0056] generate user interface data, the user interface data comprising a representation of each of the multiple short variants, wherein the representation of each of the multiple short variants comprises long variant data of the identified long variant associated with that short variant.

[0057] Optional features described of any aspect of method, computer readable medium or computer system, where appropriate, similarly apply to the other aspects also described here.

BRIEF DESCRIPTION OF DRAWINGS

[0058] An example will be described with reference to

[0059] FIG. **1** illustrates a device for presenting whole genome sequence data.

[0060] FIG. **2** illustrates a relational database for storing whole genome sequencing data.

[0061] FIG. **3** illustrates a method for presenting whole genome sequence data.

[0062] FIG. **4** illustrates a resulting short variant table.

[0063] FIG. **5** illustrates a user interface presenting whole genome sequence data.

[0064] FIG. **6** illustrates a user interface comprising multiple search options.

[0065] FIG. **7** illustrates overlapping variants.

DESCRIPTION OF EMBODIMENTS

[0066] Whole genome sequencing (WGS) has become more accessible due to a rapidly falling price tag and a shortened sequencing time facilitated by next generation sequencing (NGS) technologies. The large data sets from sequencers, such as Illumina X10, are analysed by bioinformatics software which align sequence reads to a reference genome, to identify variants, that is, differences between a reference genome and sequences of a sample genome, and which then predict effects of the detected variants on the patient. The outcome may be a prediction of an occurrence or risk of a particular disease or other traits, such as quantitative traits.

[0067] Most bioinformatics software tools are designed for specific purposes. Therefore, the output of multiple tools may be combined to arrive at a meaningful result. Some tools generate an output that can be processed by the next tool in the pipeline. In this case, the intermediate result is often of little relevance to the practical application. In other cases, multiple tools are used in parallel to obtain different outputs which are all relevant to the practical application. In particular, when the WGS data is reviewed by a human interpreter, such as a clinical pathologist, the data from multiple tools is reviewed and presented to the interpreter. This presents the difficulty that correlations between the outputs from the different tools are difficult to see. For example, it is difficult to see that a short variant in the output of a short variant caller is within a long variant in the output of a long variant caller. Identifying this relationship would enable the interpreter to draw a conclusion that would be difficult to obtain based on the short variants and long variants in isolation.

[0068] While some examples herein relate to medical applications where users of the system include clinical pathologists reviewing patient WGS data, it is to be understood that other applications are equally possible, including lifestyle genomics where personal WGS data is reviewed for

specific traits, or veterinary applications including animal breeding and artificial selection where the WGS data relates to individual animals.

[0069] FIG. **1** illustrates a device **100** for presenting whole genome sequence data of a patient such that a relationship between short variants and long variants becomes visible. The computer system **100** comprises a processor **101** connected to a program memory **102**, a data memory **103**, a communication port **110** and a user port **111**. The data memory **103** holds a file system, such as NTFS, FAT32, ext2/ext3/ext4 or others. This file system stores the whole genome sequence data of the patient.

[0070] The whole genome sequence data comprises a short variant data file **104** on the file system. The short variant data file **104** comprises short variant data related to multiple short variants of the patient at respective short variant coordinates. For example, the short variant data file **104** may be the output file generated by a short variant calling tool. Tools include, but are not limited to, one or more of GATK HaplotypeCaller, SAMtools mpileup, MuTect and Strelka.

[0071] A short variant is a region within a sequenced genome having a sequence that differs from the corresponding region of a reference genome. The reference genome may be a third party reference genome (germline variant) or may be a combination of the latter and a germline genome when sequencing tumour/somatic samples. In the latter case, called "somatic variant", the short variants are effectively the differences between the germline genome and the tumour/somatic genome. A short variant is typically between 1 and 100 bases in length. A short variant may be a Single Nucleotide Polymorphism (SNP), which is a difference between the sample genome and reference genome at one single locus, or a insertion/deletion (indel) where one or more bases are inserted or deleted from the sample genome relative to the reference genome. Each short variant is located at a short variant coordinate, which is also stored in the short variant data. The coordinate may comprise a chromosome number and the number of bases from the start of the chromosome of the reference genome or the sample genome. For example, the rs6311 variant is a SNP located in chromosome 13 and has the coordinate 13:46897343. The short variant data file may be a text file comprising a string for the SNP type, such as "C/T" for a change from cytosine to thymine and a string "13:46897343" or two numbers "13" and "46897343" for chromosome and base count from start, respectively. The data may be stored in VCF, XML, JSON or other formats including compressed, uncompressed, encrypted and unencrypted formats.

[0072] Processor **101** reads the short variant data file and may create a record in a database for each short variant. For example, the database may be a relational database, such as SQL.

[0073] FIG. **2** illustrates a relational database **200** for storing whole genome sequencing data hosted on data store **103**. Database **200** comprises a short variant table **201** comprising one record for each short variant. In this example, the short variant table **201** has a first data field **202** for chromosome number, a second data field **203** for the coordinate within the chromosome, a third data field **204** for the reference base, a fourth data field **205** for the alternative allele and a fifth data field **206** for the variant genotype. In the example of FIG. **2**, there are three short variants, that is, three SNPs in the whole genome sequencing data for this individual.

[0074] The whole genome sequence data further comprises a long variant data file **105** on the file system **103**. The long variant data file **105** comprises long variant data related to multiple long variants in the individual at respective long variant coordinates. For example, the second data file **105** may be the output file generated by one or more long variant calling tools. Long variant calling tools include, but are not limited to, one or more of CNVnator, PLINK Delly, Sequenza, BreakDancer, Manta and LUMPY.

[0075] A long variant is a region of long length within a sample genome that has been affected by a structural and/or copy number genetic variation event, or is otherwise of interest due to being affected by a normal genomic process such as recombination. A long variant ranges in size from 100 bases to hundreds of millions of bases (entire chromosomes). Similar to short variants, long variants may be somatic. That is, long variants may indicate a difference between a tumour/somatic sample and a germline sample.

[0076] A long variant may be a structural variant (SV), a copy number variant (CNV) or any region of the genome affected by a genetic process of interest. A long variant (CNV) may be a duplication/deletion. A long variant (CNV) may be an insertion. A long variant (SV) may be an inversion. A long variant (SV) may be a translocation. A region of interest may be a region of homozygosity potentially caused by consanguinity or deletion followed by duplication events in cancer.

[0077] Processor **101** reads the long variant data file and may create records in database **200** for the long variants. In one example, processor **101** creates two records for each long variant in a long variant table **211** comprising data fields for block identifier **212**, variant type **213**, chromosome number **214**, a first coordinate **215** and a second coordinate **216**.

[0078] In the example of FIG. **2**, database **200** stores a first record **217** in long variant table **211** which relates to a deletion as indicated by the "del" value in the variant data field **213**. This means, the genetic information between the first coordinate **215** and the second coordinate **216** is deleted. For copy number variants and other long variants a single record in long variant table **211** may be sufficient.

[0079] Since structural variants may only impact the break points at which they occur, and not the internal sequence, these variants can be represented by two separate records in long variant table **211**. For example, database **200** stores a second record **218** and a third record **219** to represent a single structural variation. The first data record **218** represents the imprecise start coordinates of an inversion and the second data record **219** represents the imprecise end coordinates of the inversion. In other words, for this individual, the region between 46908654 and 47867626 on chromosome 3 is inverted. Processor **101** identifies the inversion by reading the output file from the long variant calling tool and creates a link between the two data records **218** and **219** by storing a common identifier '2' in identifier field **212**. The link may also be stored in a separate link table having a block identifier field and an event identifier field. The block identifier field is a foreign key to block identifier field **212** of long variant table **211** while the event identifier field is a foreign key to a separate event table. In that case, the link table may have further data fields for long variant data that

is associated with each long variant, such that the long variant data is not duplicated in the two entries of the long variant table **211**. In particular, the link table may have a data field for variant type instead of variant type data field **213** in long variant table **211**. Similarly, processor **101** stores long variant data representing a translocation as two records with a corresponding link.

[0080] It is noted that while in the above example the data files **104** and **105** are stored on data store **103** they may equally be stored elsewhere. In particular, data files **104** and **105** may be stored on cloud storage associated with a cloud computing platform that hosts the short variant calling tool(s) and the long variant calling tool(s). For example, DNANexus may be used to execute calling tools on dynamically provisioned virtual machines and to store output files on cloud storage. Processor **101** may then receive the short variant data and long variant data over the Internet or the cloud-internal network. Equally, database **200** may be stored on cloud storage or may be a distributed database. Processor **101** can create, modify and select records in the database remotely by a remote database connection.

[0081] Returning back to FIG. **1**, computer system **100** further comprises a display device **112** to display a representation **113** of the variants stored on data store **103** to a user **114**. The program memory **102** is a non-transitory computer readable medium, such as a hard drive, a solid state disk or CD-ROM. Software, that is, an executable program stored on program memory **102** causes the processor **101** to perform the method in FIG. **3**, that is, processor **101** creates short variant records, identifies one long variant having a short variant within, adds a reference to the long variant and generates a user interface.

[0082] The processor **101** may then store the genome data on data store **103**, such as on RAM or a processor register. Processor **101** may also send the determined variants via communication port **110** to a server, such as a hospital's patient record server. The processor **101** may receive data, such as WGS data, from data memory **103** as well as from the communications port **110**. Processor **101** may receive WGS data from a DNA sequencing machine, such as an Illumina X10. This receiving step may comprise the sequencing machine storing the WGS data on cloud storage and processor **101** retrieving this data from the cloud storage.

[0083] Although communications port **110** and user port **111** are shown as distinct entities, it is to be understood that any kind of data port may be used to receive data, such as a network connection, a memory interface, a pin of the chip package of processor **101**, or logical ports, such as IP sockets or parameters of functions stored on program memory **102** and executed by processor **101**. These parameters may be stored on data memory **103** and may be handled by-value or by-reference, that is, as a pointer, in the source code.

[0084] The processor **101** may receive data through all these interfaces, which includes memory access of volatile memory, such as cache or RAM, or non-volatile memory, such as an optical disk drive, hard disk drive, storage server or cloud storage. The computer system **100** may further be implemented within a cloud computing environment, such as a managed group of interconnected servers hosting a dynamic number of virtual machines.

[0085] It is to be understood that any receiving step may be preceded by the processor **101** determining or computing the data that is later received. For example, the processor **101** determines WGS data and stores that data in data memory **103**, such as RAM or a processor register. The processor **101** then requests the data from the data memory **103**, such as by providing a read signal together with a memory address. The data memory **103** provides the data as a voltage signal on a physical bit line and the processor **101** receives the whole genome data via a memory interface.

[0086] It is to be understood that throughout this disclosure unless stated otherwise, nodes, edges, graphs, solutions, variables, records, variants, coordinates and the like refer to data structures, which are physically stored on data memory **103** or processed by processor **101**. Further, for the sake of brevity when reference is made to particular variable names, such as "coordinate" or "variant" this is to be understood to refer to values of variables stored as physical data in computer system **100**.

[0087] FIG. **3** illustrates a method **300** as performed by processor **101** for presenting WGS data of a patient. FIG. **3** is to be understood as a blueprint for the software program and may be implemented step-by-step, such that each step in FIG. **3** is represented by a function in a programming language, such as PHP, C++ or Java. The resulting source code may then compiled and stored as computer executable instructions on program memory **102** or in the case of PHP or JavaScript stored directly as computer executable instructions on program memory **102** without compilation.

[0088] Processor **101** creates **301** a data record in the database **200** for each of the multiple short variants as described above with reference to FIG. **2**. Then, processor **101** identifies **302** for each of the short variant coordinates one of the multiple long variants where that short variant coordinate lies within the coordinates of the one of the multiple long variants. In one example, processor **101** executes two nested loops where the outer loop iterates over all short variants in short variant table **201** and the inner loop iterates over all long variant identifiers in long variant table **211** for the current short variant from the outer loop. Processor **101** checks whether the current short variant coordinate **202** is greater or equal than the start coordinate in first record **215** and less than or equal to the end coordinate in second record **216** of the current long variant. If this comparison is true, processor adds **303** to the data record of that short variant a reference to the identified one of the multiple long variants.

[0089] In another example, processor **101** sorts the short variants and the long variants by coordinate. This way, the processor **101** can abort the search earlier and commence the search in the long variant table where it stopped for the previous short variant to accelerate the process.

[0090] In yet another example, processor **101** performs a database function, such as a JOIN function based on the coordinates to exploit the optimised database routines. In particular, these coordinates are used as the INNER JOIN condition for searching the blocks. Database **200** stores a genes table with records that link genes to coordinates where each gene->coordinates event has an ID. Processor **101** queries this table for a gene list, which returns all the gene->coordinate IDs. These IDs can then be used to search the block table **211** where the start and end of the block overlaps at all with the coordinates of each of the gene->coordinate IDs returned before. This overlap condition may be included as a WHERE clause into the SELECT statement.

[0091] FIG. **4** illustrates a resulting short variant table **400** comprising the data fields from short variant table **201** in FIG. **2** for chromosome number **202**, coordinate within the chromosome **203**, reference base **204**, alternative allele **205** and variant genotype **206**. In addition, short variant table **400** now comprises a long variant ID field **401**. In this example, processor **101** determines that short variant coordinate 46897343 is greater than long variant start coordinate 46896343 and less than long variant end coordinate 46898124. Therefore, processor **101** adds to data record **402** of this short variant a reference to the identified long variant by including the identifier '1' of the long variant in long variant table **211**. This way, processor **101** creates an association between the short variant and the identified long variant. In SQL terms, processor **101** enters a foreign reference into table **400** and the foreign reference relates to a long variant. It is noted that table **400** does not need to be a table in the database but can be a table on a user interface as explained below. In that case, the long variant ID field **401** may contain more information about the long variant than only the reference identifier.

[0092] FIG. **5** illustrates a user interface **500** presenting whole genome sequence data which the processor **101** generates **304** on the display device. The user interface **500** comprises a representation of the multiple short variants. For example, the representation may be a list of the multiple short variants. The representation may be a table **500** of the multiple short variants. The representation of the multiple short variants comprises long variant data of the long variant according to the reference from the data record for each of the multiple short variants. In other words, processor **101** retrieves the short variant data from table **400** and for each short variant, processor **101** retrieves the long variant data using the identifier in the long variant ID field **401** as a key. Processor **101** then includes the long variant data into the representation.

[0093] Generating the user interface may comprise generating user interface data, such as by writing HTML code to a HTML file that is later rendered remotely by an internet browser. Generating the user interface may also comprise sending user interface data directly to the browser, such as through JavaScript methods. This may include the use of GET and POST methods and XMLHttpRequest data. For example, the JavaScript method may send filter settings and request a list of short variants to a Software as a Service (SaaS) platform. The SaaS platform responds by sending the list of short variants where each item in the list is a representation of a short variant and may include the long variant data. The JavaScript method can then iterate over the received list object and create a table row for each item in the list object. This may be performed within an AJAX framework or an Angular frontend connected to a Flask backend.

[0094] In the example of FIG. **5** table **500** of the short variants comprises a gene name column **501**, a chromosome column **502**, a coordinate column **503**, a reference base column **504**, an alternative allele column **505**, a genotype column and a long variant data column **507**. Table **500** may comprise a locus name column in addition to or instead of the gene name column **501** for situations where a region in the genome is defined and labelled by a name but a gene is not known or not directly associated with that region. In the example of FIG. **5**, only the first variant **510** was found in a long variant coordinate range. As a result, processor **101** adds long variant data into column **507**. In this example, processor **101** adds the string 'inv' from table **211** in FIG. **2** to indicate to the user that variant **510** is located within a region that is also the subject of an inversion event.

[0095] Database **200** may comprise a separate gene table. This gene table comprises data fields for a gene identifier, such as "BRCA1" and the corresponding gene coordinates including a start and an end coordinate. The gene table may comprise a data field for a gene description, associated diseases and other information. Processor **101** may query the gene table when generating the user interface table **500** and include the gene information into the table in the gene column **501**. In order to optimise performance, processor **101** may perform an SQL JOIN statement between the gene table, the long variant table and the short variant table with the coordinates as the common key.

[0096] It is noted that table **500** may contain more or less columns than shown in FIG. **5**. For example, table **500** may not have the coordinate column **503** in applications where users are unlikely to be able to interpret the large numbers typically associated with coordinates. On the other hand, table **500** may comprise further columns indicative of associations between a short variant and a disease or other traits or phenotypes.

[0097] In one example, long variant data column **507** shows the entire output generated by the long variant calling tool for the identified long variant, such as the coordinate range.

[0098] A user, such as a clinical pathologist, can then review the list of short variants and can conveniently see for each short variant whether that short variant is also nested within a long variant, such as a structural variant. This allows the user to draw more accurate conclusions from the WGS data, such as a more accurate diagnosis. In cases where only a small number of qualified users are available for a large number of patients, the proposed system allows the user to perform their duties more efficiently and help more patients than otherwise possible.

[0099] Processor **101** may execute multiple different long variant calling tools to generate multiple long variant data files. This may be useful when there are multiple long variant calling tools available and each tool has particular advantages or can call different types of long variants. In this case, processor **101** repeats the steps of identifying **302** for each one of the multiple long variants and adding **303** to the data record for each of the multiple second data files. Long variant data column **507** in FIG. **5** may then comprise a concatenation of the output data from the different long variant calling tools.

[0100] Processor **101** may also generate a filter interface on display device **112** to allow the user to reduce the number of short variants that are displayed in representation **500**. The filter interface may comprise multiple different filters. The filters may comprise a gene name filter where a user can enter or select the name of one or more genes and processor **101** includes only variants within the entered or selected one or more genes. More particularly, processor **101** may query the gene table to retrieve all sets of chromosome, start and end coordinates of a selected gene and then determine which variants are within these coordinates. The user may be aware of an association between certain genes and observed traits and therefore, it is useful for the user to limit the output to those genes.

[0101] Similarly, the filters may also include a gene coordinate filter such that processor **101** only includes variants that lie within a provided coordinate range.

[0102] The filters may also include an overlap filter. In this case, processor **101** determines whether the coordinate range of a long variant overlaps with the coordinate range of any other long variant and only includes those long variants if they overlap. Overlaps may be pairwise, between samples or between long variant types/methods within a given set of samples and variant types/methods.

[0103] In one example, the short variant data and the long variant data relate to multiple samples, that is, multiple patients or subjects. In this case, the data tables **201** and **211** may comprise an additional data field for a sample identifier. The sample identifier of the WGS data may then serve as a common key between the short variant table and the long variant table. In other words, processor **101** can group the variants by the sample identifier or only retrieve variants that relate to a particular sample. Further, processor **101** can determine which long variants overlap between samples. This may apply to the use case of a single long variant calling tool and the overlap filter is configured by the user to only show long variants that overlap, which means individuals have long variants at similar positions. This may be useful when investigating inherited traits where the ancestors and the offspring share the same long variant that may be responsible for that trait, such as in the case of a heritable disease.

[0104] FIG. **6** illustrates a user interface **600** comprising multiple search options. User interface **600** comprises a database identifier **601** to indicate to the user which database is currently selected. It is noted that the database may hold variant data related to multiple individuals, such as multiple family members. User interface **600** further comprises a family selector **610** including options for the entire dataset **611**, a particular family **612** labelled 'D' or proceed without specifying a family **613**. It is noted that in cases where the selected database comprises variant data of multiple families, the selector button **612** would be replicated for each family with a respective label replacing 'D' in FIG. **6**. Processor **101** receives the selection of the family through selector **610**, retrieves family information from the database and displays that information in a family information text field **620**, such as for each individual family member whether that individual is affected.

[0105] User interface **600** further comprises an analysis type selector **630** where the user can choose between gene lists **631**, overlapping blocks **632** and genomic coordinates **633**. Ultimately, the goal of these queries is to obtain a list of genomic blocks that match specific criteria for a set of samples. Upon receiving the selection of querying gene lists **631**, processor **101** displays all blocks for all selected samples that overlap with any of the genes in one or more gene lists specified. Upon receiving the selection of overlapping blocks **632** processor **101** displays blocks for all selected samples that overlap by one or more bases. Upon receiving the selection of genomic coordinates **633**, processor **101** displays blocks for all selected samples where a block overlaps with one or more samples at one or more bases.

[0106] User interface **600** further comprises a selectable gene list **640** where a user can select one or more genes from that list. Processor **101** receives the selection from user interface **600** and limits the listed variants to those that fall within the selected genes. User interface **600** also comprises a custom gene list **645** where a user can type or paste gene names directly with the same effect as selecting the genes manually in selectable gene lest **640**. A submit button **650** causes the processor **101** to retrieve the entered data from user interface **600**, perform the corresponding query and list the resulting variants as described herein.

[0107] FIG. **7** illustrates overlapping variants in more detail where the horizontal direction represents the gene coordinate. In this example, database **200** stores long variant data and short variant data of three samples. A first sample **701** has a long variant **702** and four short variants **703**, **704**, **705** and **706**, respectively. A second sample **710** has second long variant **711** and two short variants **712** and **713** corresponding to short variants **704** and **705**, respectively. In other words, individuals corresponding to samples **701** and **710** share the same short variants **704**/**712** and **705**/**713**. A third sample **720** has third long variant **721**. As can be seen in FIG. **7**, first long variant **702** overlaps with second long variant **711**. Short variants **703** and **704** are within first long variant **702** but only short variant **704** (as short variant **712**) is also within overlapping long variant **711**. As a result, activating the overlap filter will cause processor **101** to show only the short variant **704**/**712** as this short variant is within the region of the long variant **702** that overlaps with another long variant **711** from a different sample. In other words, when restricting variants based on overlaps of blocks, processor **101** returns short variants that are present in both individuals and also in overlapping blocks, i.e. the block was inherited with the short causative variant within it.

[0108] Short variants **703**, **705** and **706** are not within the region of overlap between long variants **702** and **711** and are therefore excluded from the results. The third long variant **721** does not overlap with any of the other long variants and any short variants (not shown) within third long variant **721** are also excluded. The overlap filter allows the user to view only long variants that are common between different samples, which can reduce the number of variants significantly.

[0109] Processor **101** may apply the overlap filter as described above for different long variant calling tools such that the three samples **701**, **710** and **720** are replaced by the output of three long variant calling tools.

[0110] The long variant data may comprise inheritance data. For example, the long variant table **211** may comprise a data field for inheritance. Inheritance information may be stored with the short variants or stored in a central table separate to both short and long variants. In one example, stored information comprises affected/unaffected status and male/female/unknown gender. Dominant/recessive/compound inheritance predictions may be stored as part of the phenotype data for the patient/family and may be stored in an external database. Data values may include autosomal dominant, autosomal recessive, compound heterozygous and de novo dominant. Processor **101** can then perform an inheritance filter such that only those short variants are shown where the corresponding long variant has a user-specified inheritance value. The inheritance value may be generated by an inheritance analyser, such as GEMINI.

[0111] The long variant data may comprise copy number data. For example, the long variant table **211** may comprise a data field for copy number. Data values may be numeric or NULL where no copy number estimate was made. Processor **101** can then perform a copy number filter such that only

those short variants are shown where the corresponding long variant has a user-specified copy number. The copy number value may be generated by a long variant detection tool.

[0112] By applying these filters in different combinations a user can interactively reduce the number of variants for the particular individual. This allows the user to make full use of the available WGS data and derive conclusions or diagnoses that would otherwise have been difficult if not impossible to derive.

[0113] It is noted that processor **101** may also operate on the long variants only without reference to the short variants. In this case, processor **101** may filter the long variants by overlapping long variants from different samples and/or different individuals. For example, a user could ask what are the genes within overlapping blocks of regions of homozygosity in the affected samples in a given family and the output would be long variants and the genes within them only.

[0114] It will be appreciated by persons skilled in the art that numerous variations and/or modifications may be made to the specific embodiments without departing from the scope as defined in the claims.

[0115] It should be understood that the techniques of the present disclosure might be implemented using a variety of technologies. For example, the methods described herein may be implemented by a series of computer executable instructions residing on a suitable computer readable medium. Suitable computer readable media may include volatile (e.g. RAM) and/or non-volatile (e.g. ROM, disk) memory, carrier waves and transmission media. Exemplary carrier waves may take the form of electrical, electromagnetic or optical signals conveying digital data steams along a local network or a publically accessible network such as the internet.

[0116] It should also be understood that, unless specifically stated otherwise as apparent from the following discussion, it is appreciated that throughout the description, discussions utilizing terms such as "estimating" or "processing" or "computing" or "calculating", "optimizing" or "determining" or "displaying" or "maximising" or the like, refer to the action and processes of a computer system, or similar electronic computing device, that processes and transforms data represented as physical (electronic) quantities within the computer system's registers and memories into other data similarly represented as physical quantities within the computer system memories or registers or other such information storage, transmission or display devices.

[0117] The present embodiments are, therefore, to be considered in all respects as illustrative and not restrictive.

1. A device for presenting whole genome sequence data of a patient, the device comprising:

a file system to store the whole genome sequence data of the patient, the whole genome sequence data comprising:

a first data file comprising short variant data related to multiple short variants in the patient at respective short variant coordinates;

a second data file comprising long variant data related to multiple long variants in the patient at respective long variant coordinates;

a database to store variant data as data records;

a display device to display a representation of variants; and

a processor configured to

create a data record in the database for each of the multiple short variants,

identify for each of the short variant coordinates one of the multiple long variants where that short variant coordinate lies within the coordinates of the one of the multiple long variants,

add to the data record of that short variant a reference to the identified one of the multiple long variants, and

generate a user interface on the display device, the user interface comprising a representation of the multiple short variants, wherein the representation of the multiple short variants comprises long variant data of the long variant according to the reference from the data record for each of the multiple short variants.

2. The device of claim **1**, wherein the processor is further configured to execute a short variant calling tool to generate the first data file and a long variant calling tool to generate the second data file.

3. The device of claim **2**, wherein the long variant calling tool generates annotation data for each long variant and the reference to the long variant comprises the annotation data.

4. The device of claim **3**, wherein the processor is further configured to:

repeat the step of executing a long variant calling tool for multiple different long variant calling tools to generate multiple second data files; and

repeat the steps of identifying one of the multiple long variants and adding to the data record for each of the multiple second data files.

5. The device of claim **4**, wherein the reference to the long variant comprises a concatenation of the annotation data from the multiple long variant calling tools.

6. The device of claim **4**, wherein the database comprises a long variant table to store long variants from the multiple long variant calling tools as separate rows.

7. The device of claim **1**, wherein the processor is further configured to:

identify an inversion in the whole genome sequence data based on the long variant data; and

create two data records in the database to represent the inversion.

8. The device of claim **1**, wherein the processor is further configured to:

identify a translocation in the whole genome sequence data based on the long variant data; and

create two data records in the database to represent the translocation.

9. The device of claim **7**, wherein creating two data records comprises creating a link between the two data records.

10. The device of claim **7**, wherein the database is a relational database comprising a table to store links between the two data records.

11. The device of claim **1**, wherein the database comprises a short variant table to store short variants and a long variant table to store long variants and a sample identifier of the whole genome sequence data serves as a common key between the short variant table and the long variant table.

12. The device of claim **11**, wherein the database comprises a gene table to store gene information, wherein the gene information comprises a gene identifier and gene coordinates.

13. The device of claim **12**, wherein the short variant table comprises short variant coordinates and the long variant table comprises long variant coordinates and the short variant coordinates, long variant coordinates and gene coordinates serve as a common key between the short variant table, the long variant table and the gene table.

14. The device of claim **1**, wherein the processor is further configured to filter the short variant data based on the long variant data.

15. The device of claim **14**, wherein the processor is further configured to filter the short variant data based on an overlap between long variants of different samples and/or long variant calling tools.

16. The device of claim **14**, wherein the processor is further configured to filter the short variant data based on Mendelian inheritance associated with the genomic data.

17. The device of claim **14**, wherein the processor is further configured to filter the short variant data based on copy number data associated with the long variant data.

18. A method for presenting whole genome sequence data of an individual, the method comprising:

receiving the whole genome sequence data of the individual, the whole genome sequence data comprising:

short variant data related to multiple short variants of the individual at respective short variant coordinates; and

long variant data related to multiple long variants of the individual at respective long variant coordinates;

identifying for each of the short variant coordinates one of the multiple long variants where that short variant coordinate lies within the coordinates of the one of the multiple long variants;

creating an association between that short variant and the identified one of the multiple long variants; and

generating user interface data, the user interface data comprising a representation of each of the multiple short variants, wherein the representation of each of the multiple short variants comprises long variant data of the identified long variant associated with that short variant.

19. Software that, when installed on a computer, causes the computer to perform the steps of:

receiving the whole genome sequence data of the individual, the whole genome sequence data comprising:

short variant data related to multiple short variants of the individual at respective short variant coordinates; and

long variant data related to multiple long variants of the individual at respective long variant coordinates;

identifying for each of the short variant coordinates one of the multiple long variants where that short variant coordinate lies within the coordinates of the one of the multiple long variants;

creating an association between that short variant and the identified one of the multiple long variants; and

generating user interface data, the user interface data comprising a representation of each of the multiple short variants, wherein the representation of each of the multiple short variants comprises long variant data of the identified long variant associated with that short variant.

20. (canceled)

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