

SERVIZIO SANITARIO REGIONALE
EMILIA - ROMAGNA
Istituto Ortopedico Rizzoli di Bologna
Istituto di Ricovero e Cura a Carattere Scientifico



GePhCARD & BioMIMS:

**a combined platform that support research
on hereditary diseases**

October 14th – NETTAB 2011

Marina Mordenti – Rizzoli Orthopaedic Institute



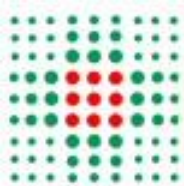
**Difficulty &
delay in
diagnosis**

**No data
exchange**

- Partial data gathering
- No data integration
- Reduced data merging
- Few information

**No statistical
analyses**

**Inadequate
treatments**



Increase knowledge on Hereditary Diseases

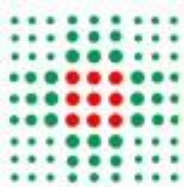
- collect clinical and genealogical data of each patient /family
- increase molecular screening on blood/tissue samples

Our focus is to define a correlation between clinical data (**Phenotype**) and genetic screening (**Genotype**)



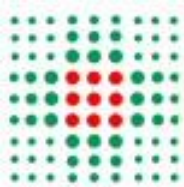
Short overview on Hereditary Rare Diseases

- less than one in 2000
- 25 million people are affected by them
- 7000 diseases are rare
- Most involve skeleton
- Mostly are not curable, chronic, life-threatening



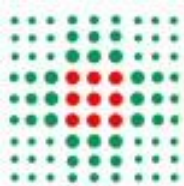
Multiple Osteochondromas - MO

- cartilaginous caps on long bones
- huge inter/intra-familial clinical variability (3 class each divided in 2 sub-class)
- in less than 5% of the patients a progression into a SPC
- Mutations on EXT1/EXT2 genes
- Mutated proteins for bone growth



Osteogenesis Imperfecta - OI

- heterogeneous disorder
- susceptibility to fracture, bone fragility
- 4 clinical types, expanded into 7
- caused by mutations in COL1A1 or COL1A2 genes
- mutated chains of type I collagen, structural protein of bone



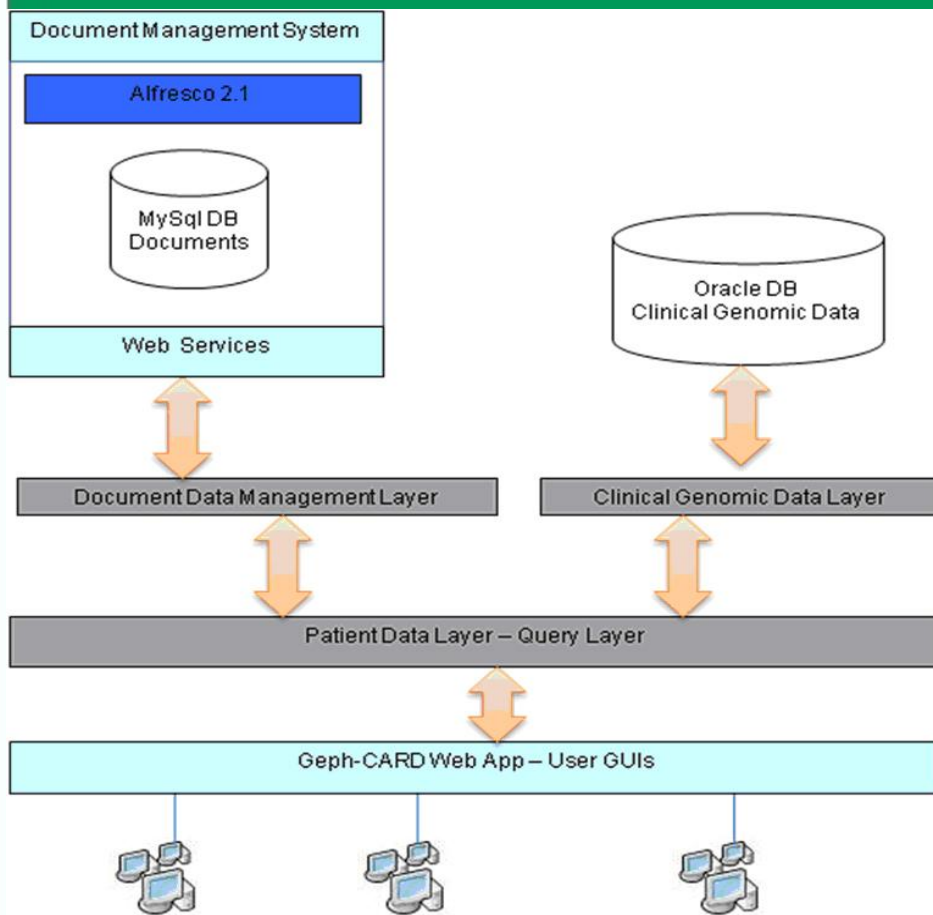
IT FOR SUPPORTING REASERCH IN HRD

- **Store genomic data**
- **Store clinical data**
- **Create a data model to integrate clinical and genomic data in a standard way to allow heterogeneous application interoperability**
- **Correlate genomic data to clinical data in a patient centric view**



GePhCARD: IT PLATFORM FOR COLLECTION

designed as services (Web Services) and developed according to SOA principles



a relational database to store clinical, genomic and genealogic data of patients

a relational database to store and index digital documents

a document management system based on Alfresco 2.1 framework

a web application



GePhCARD: IT PLATFORM FOR COLLECTION

- **GENEALOGICAL DATA DOMAIN**

To store general information on each family and to guarantee the possibility to compare clinical and genomic data inside the same family

- **PERSONAL DATA DOMAIN & PATIENT PANEL**

To store a complete set of private data for each patient or relative. Some fields are mandatory to identify each patient univocally



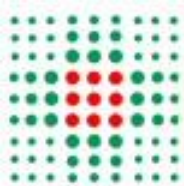
GePhCARD: IT PLATFORM FOR COLLECTION

- **CLINICAL CHART**

2 sections: a left navigation panel structured as a tree with data distributed in sub-sections and a right section created to visualize the sub-section's details

- **DOCUMENTAL DATA DOMAIN**

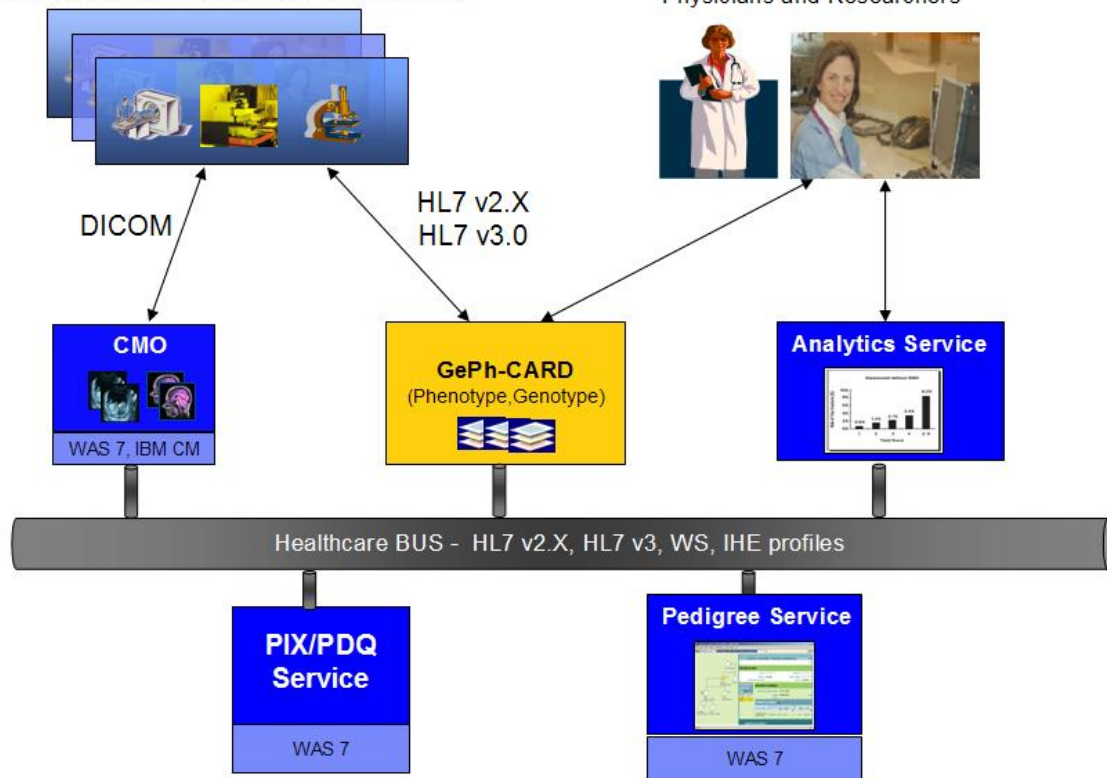
an existing professional open source CMS Alfresco for storing document and a full index based searching system to perform both full text and metadata searches way



BIOMIMS: IT PLATFORM FOR COLLECTION

Hospitals (PACS, Clinical and Genetic Labs)

Physicians and Researchers



**relational DB for archiving
clinical and genetic data**

**a Light MPI Server (Master
Patient Index) for
interoperability**

**a Content Manager for storage
of clinical and genetic raw data**

**an innovative tool for pedigree
analysis and clustering**

a Web based UI interface

**a Medical Imaging Repository (CMO) (secure DICOM based
communication)**



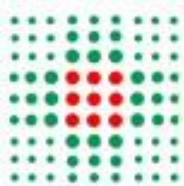
BIOMIMS: IT PLATFORM FOR COLLECTION

DICOM COMUNICATION

To collect and integrate medical images (upload and retrieve from the appropriate system service in DICOM format)

MASTER PATIENT INDEX

To ensure the correct identification of patients and their data in a standard manner



BIOMIMS: IT PLATFORM FOR COLLECTION

PATIENT IDENTIFIER

IHE patient identifier Cross-Reference (PIX) and Patient Demographic Query (PDQ) transactions. To enable interoperability and cross-institutional information sharing (preserving security and privacy)

PEDIGREE ANALYTICS

to manage genealogic trees for an healthcare related pedigree creation, management and analysis



GePhCARD & BioMIMS

They work in concert to:

- **collect** data
- support a set of sophisticated and **federated queries** (include a combination of different types of information)
- **store** interesting queries
- **extrapolate** data
- **analyse** data



PATIENT DATA ACCESSIBILITY

» GephCard - orto20 orto20 (Bologna - 20) - Orthopedician - DEMO

Patients Families Statistics Options

X OIS0001 - 30 - 3000000001

List of patients: Row 1 of 6

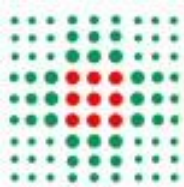
	Lab. ID	Surname	Name	Family Id	Gender	Birth Date			
↔	OIS0001	NERI	FRANCO	NERI(3)	MALE	01/01/1944	<input checked="" type="checkbox"/>	<input type="checkbox"/>	OSPEDALE PADOVA - 30
↔	FEYS0004	NERI	MARIA	ROSSI(1)	FEMALE	01/01/1951	<input type="checkbox"/>	<input type="checkbox"/>	OSPEDALE MODENA - 10
↔	FEYS0003	ROSSI	FRANCO	ROSSI(2)	MALE	01/01/1943	<input checked="" type="checkbox"/>	<input type="checkbox"/>	OSPEDALE BOLOGNA - 20
↔	FEYS0003	ROSSI	FRANCO	ROSSI(1)	MALE	01/01/1943	<input type="checkbox"/>	<input type="checkbox"/>	OSPEDALE MODENA - 10
↔	FEYS0002	ROSSI	MARIO	ROSSI(1)	MALE		<input type="checkbox"/>	<input type="checkbox"/>	OSPEDALE MODENA - 10
↔	FEYS0001	ROSSI	PAOLA	ROSSI(1)	FEMALE		<input checked="" type="checkbox"/>	<input type="checkbox"/>	OSPEDALE MODENA - 10
↔							<input type="checkbox"/>	<input type="checkbox"/>	



PATIENT'S FAMILY INTERFACE

The screenshot displays a software interface for managing family data. On the left, a 'List Of Families' panel shows a tree view for the 'ROSSI' family, with two members listed: 'PAOLA ROSSI (1000000001)' and 'MARIO ROSSI (1000000002)'. A context menu is open over Mario Rossi, offering options: 'Delete', 'View Pedigree', 'Clinical and genomic information', and 'View allowed operations'. The main area is titled 'Person Details' and shows a 'DATA CHANGED' notification. The form contains the following fields:

Person Code	10002	Lab. ID	1000000002
Patient Code		I.C.C. ID	1000000002
Name	MARIO	Notes	
Surname	ROSSI		
Gender	MALE		
Family Name	ROSSI		
Proband	<input type="checkbox"/> Affected	<input checked="" type="checkbox"/> Alive	<input checked="" type="checkbox"/>
Relation. vs Prob	SIBILING		
Parent (no prob.)			



PATIENT PANEL

Genotype Phenotype Laboratory - Microsoft Internet Explorer

File Modifica Visualizza Preferiti Strumenti ?

Indietro - - - - - Cerca Preferiti - - - - - Vai Collegamenti >>

Indirizzo http://localhost:8888/Gephcard/Gephcard.htm

Google G - - - - - Cerca - - - - - Segnalibri - - - - - Pop-up OK - - - - - Controllo - - - - - Impostazioni - - - - -

< Genotype Phenotype Laboratory cmd: []

> General Data Welcome DEMO1 DEMO1! You are logged in as USER ENTE

> Administration

Open display.

> Patient Data

Family Data

List Of Patients

List Of Users

Close all

SEARCH: Row (line) 1 of 1

id	FEX59999	Family	ARAGONESE - ARAGONESE
Name	MARIO	Surname	ARAGONESE

PATIENT NAVIGATOR

- PERSONAL INFO
- PRE-DIAGNOSES
- DIAGNOSES
- VISITS
- SAMPLES
- GENETIC ANALYSES
- CLINICAL OBSERVATIONS
- DOCUMENTS

PERSONAL INFO

PERSONAL INFO

Personal Data and Contacts Clinical notes and Family Data

Lab. Id FEX59999 Code 606 Gender male

Name [] Surname [] Prenatal

Alive Cause of decease []

Birth Date []

Birth Place Italy City AVELLINO

Town ALTAVILLA IRPINA

Fiscal Code []

Health Insurance Card []

Contacts and Addresses

Country Italy City AREZZO

Town BUCINE

Address []

Zip Code []

Phone [] Mobile Phone []

E-mail []

TS:3734, KB:45-4 Intranet locale

patient search panel

patient navigator
tree



PATIENT PANEL

Genotype Phenotype Laboratory - Microsoft Internet Explorer

File Modifica Visualizza Preferiti Strumenti 2

Indietro - - - - - Cerca Preferiti

Indirizzo http://localhost:8888/Gephcard/Gephcard.htm

Google

< Genotype Phenotype Laboratory

> General Data Welcome DEMO1 DEMO1! You are logged in

> Administration

Open display.

> Patient Data

Family Data

List Of Patients

List Of Users

Close all

Current patient: [X]

SEARCH: Row (line) 1 of 1

id	FEX59999	Family	AR
Name	MARIO	Surname	AR

PATIENT NAVIGATOR

- PERSONAL INFO
- PRE-DIAGNOSES
- DIAGNOSES
- VISITS
- SAMPLES
- GENETIC ANALYSES
- CLINICAL OBSERVATIONS
- DOCUMENTS

TS:3734, KB:45-4

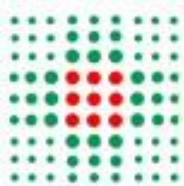
patient
t

1000000001 - 10 - 1000000001

Patient Tree: [refresh] [person] [calendar] [document]

- PERSONAL INFO
- PRE-DIAGNOSES
 - 24/05/2010 MULTIPLE OSTEC...
- DIAGNOSES
 - 24/05/2010 MULTIPLE OSTEC...
- VISITS
- CLINICAL OBSERVATIONS
 - MULTIPLE OSTECHONDROMAS
 - 24-05-2010
 - 01-01-2007
- SAMPLES
- GENETIC ANALYSES
- MEDICAL IMAGES
- DOCUMENTS

patient search panel



PERSONAL DATA DOMAIN

Genotype Phenotype Laboratory - Patient Pop Up -- Finestra di dialogo pagina Web

✓ **✗** Patient Pop Up

i Patient: The changes of the data have been registered on the database.

Patient: Revised data.

- Identification Info

Laboratory Id	FEX59999	Name	Mario	Surname	
Patient Code		Prenatal	<input type="checkbox"/>	Alive	<input checked="" type="checkbox"/>
Gender	male	Birth Date		Cause of Decease	
Birth Place	Italy	City	AVELLINO	Town	ALTAVILLA IRPINA
Fiscal Code		Health Insurance Card			

- Contacts and Addresses

Country	Italy	City Of Residence	AREZZO	Town	BUCINE
Address				Zip Code	
Phone		Mobile Phone		E-mail	

- Some clinical Notes

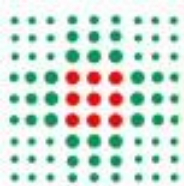
Institutional Clinical Chart Id	ZQ465546729
Other Diseases	
Notes	

- Family Data

Proband	<input checked="" type="checkbox"/>	Family Name	
---------	-------------------------------------	-------------	--

Personal data

Family data



DICOM IMAGES

Patient Tree:

- PRE-DIAGNOSES
 - 24/05/2010 MULTIPLE OS
- DIAGNOSES
- VISITS
- CLINICAL OBSERVATIONS
- MEDICAL IMAGES**
- DOCUMENTS

IBM Content Management Offering Client D1 | Sign Out

Request [Clear](#) [Search](#)

Patient ID Date of Birth X Modality US CT MR DR Sex Male
Patient Name Date From X SC DX RF NM Female
Accession # Date To X CR XA PX OT Other

Results Found 4 images [Download](#)

- 10.11.09.1975.00987654321 [MARIC]
 - 2009-12-16
 - CR #1
 - #1
 - 2009-12-14
 - 10.11.09.1975.00987654322 [SOPH]

Properties **Image** **Stream**

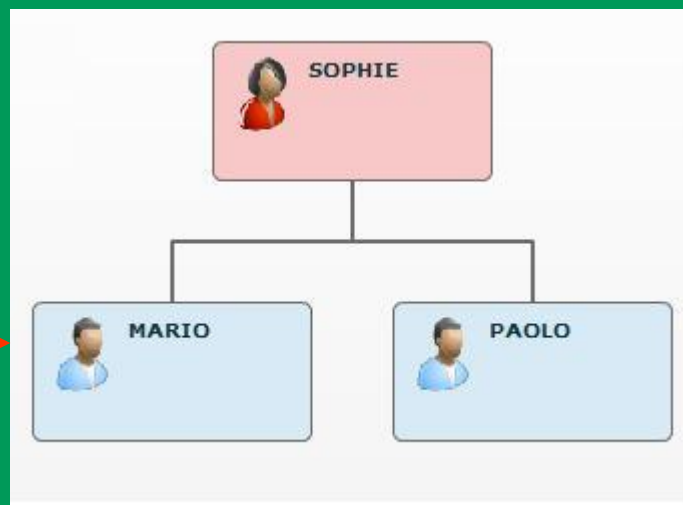


PEDIGREE TOOL

Family Data

List Of Families: Reload New

- ROSSI (1)
 - PAOLA ROSSI (1000000001)
 - MARIO ROSSI (1000000002)
 - Delete
 - View Pedigree**
 - Clinical and genomic information
 - View allowed operations





OI CLINICL DATA

ALL
DETAILS (as OI)

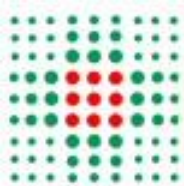
DETAILED OBSERVATIONS: Row 1 of 1

Date	23/11/2009	Disease	OSTEOGENESIS IMPERFECTA	N° of fractures	<input type="text"/>
Deafness	YES	Details	<input type="text"/>	Sclera	<input type="text"/>
Dentin. Imper.	<input type="text"/>	Details	<input type="text"/>		
Cutis Laxa	<input type="text"/>	Skin	<input type="text"/>	R. C. Def.	<input type="text"/>
Card. Lesions	<input type="text"/>	Details	<input type="text"/>	Rhizomely	<input type="text"/>
Worm. Bones	<input type="text"/>	Sp. Def.	KYPHOSIS	Frn. Boss.	<input type="text"/>
Triang. Facies	<input type="text"/>	Max. Def.	<input type="text"/>	Jn. Hyperl.	<input type="text"/>
BD	<input type="text"/>	Z Score	<input type="text"/>	T Score	<input type="text"/>
BMD	<input type="text"/>				<input type="text"/>
Notes	Dall'89 ha avuto fratture multiple in seguito a traumi diretti (anche se di lieve entità)				
Height	<input type="text"/>	Weight	<input type="text"/>	Height Percentile	<input type="text"/>

Sites - Locations - Sides
Limitations

Sites - Locations - Sides: Row 1 of 3

Site	N°	Age	Location	Side	N° fractures	Level of pain
RIBS			UNKNOWN	unknown		
HUMERUS			UNKNOWN	unknown		



ALFRESCO

Patient Tree:

- PERSONAL INFO
- PRE-DIAGNOSES
 - 24/05/2010 MULTIPLE OSTEC...
- DIAGNOSES
 - 24/05/2010 MULTIPLE OSTEC...
- VISITS
- CLINICAL OBSERVATIONS
 - MULTIPLE OSTECHONDROMAS
 - 24-05-2010
 - 01-01-2007
- SAMPLES
- GENETIC ANALYSES
- MEDICAL IMAGES
- DOCUMENTS
 - ROOT FOR DOCUMENTS
 - CLINICAL PICTURES
 - MY CLINICAL PICTURE
 - IMA Add sub folder
 - CLI Remove folder
 - GEN Upload file

Copia in corso...

Copia di E-EXML-1.xml su
<http://NSI-SERGIO:8889/alfresco/webdav/GENOTYPE-PHENOTYPE>

<http://NSI-SERGIO:8889/alfresco/webdav/>

File Modifica Visualizza Preferiti Strumenti ?

Indietro Cerca

Indirizzo <http://NSI-SERGIO:8889/alfresco/webdav/> Vai

CLINICAL FILES CLINICAL PICTURES GENETIC FILES IMAGING

igMageExtractor\MAGEMPL_EXP

Indietro Cerca

C:\TagMageExtractor\MAGEMPL_EXP

- fi_20060704_Hela1bis_U133A.xml
- ML-1.xml
- XP-136.xml
- BM-23.xml
- BM-41.xml
- BM-42.xml
- BM-46.xml
- BM-47.xml
- ETABM-48.xml
- Familial_Cancer_Associated_with_A_polymorphism...



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EMILIA - ROMAGNA

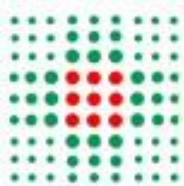
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RARE HEREDITARY DISEASES

**Lack of data
for meaningful research**

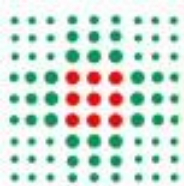
**Collaboration
among centres**



IT PLATFORM FOR COLLABORATION

The data accessibility

- **Role Based Access Control (RBAC) system**
- enables users from different organizations with customized access rights to patients' information according the user profile or role



GePh-CARD

Genotype-Phenotype
Correlation,
Analyses, Research
Database



IT PLATFORM



to **organize and screen**
genetic, genealogical,
and clinical data



genotype-phenotype
patient
characterization to a
**personalized
healthcare vision**



BioMIMS

BioMarker Imaging
Management
System



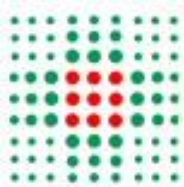
IT PLATFORM



to **merge** information
from dispersed hospitals
(pedigree, imaging, etc)

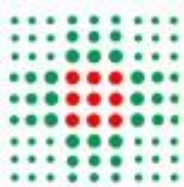


clinical and genealogical
characterization to a
**personalized healthcare
vision**



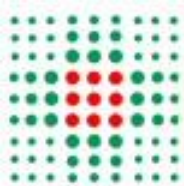
MO RESULTS

1. Male patients have more severe manifestations than female, from an inter- and an intra-familial point of view
2. EXT1 mutations are associated with a more severe form and correlate to specific clinical manifestations
3. Class III patients usually have low height
4. Negative Familiarity refers to Class III



OIS RESULTS

- 1. Quantitative genetic defects (Frameshift, Duplication, Initiating methionine, Nonsense, SpliceSite, SpliceVariant) are usual for Class I patients**
- 2. Qualitative genetic defects (In-frame insertion, In-frame deletion, In-frame insertion-deletion, Missense) are usual for Class II**



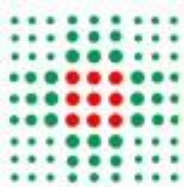
OUTCOMES 1

- More accurate and precise data → A statistical analyses dataset → Better **disease overview** and help in **differential diagnosis**
- Increased patient and family dataset → **Genotype-Phenotype Correlation** & Study on Hereditary
- Patient-Centric & Family-Centric Approach → **Patient's quality of life**



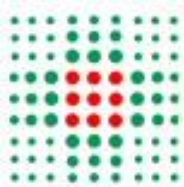
OUTCOMES 2

- Logging tool thorough an authentication system → Multilevel access profile system (different roles - different domains - different datasets) → **Data Legal Protection**
- Web-accessibility (user-friendly interface) → **Input from different locations**
- Service Oriented Architecture (SOA) → Possibility of **future implementations** and incorporations of configurable modules → Pairing of new techniques & new modules



OUTCOMES 3

- To purpose innovative research directions → To decide the future **health-related strategies**
- Multi-language engine and multi-organization structure → Increased gathering of data and **data merge**
- Advanced algorithms → Correlation patterns → **Pedigree analytics**
- Articulated **queries system** → Possibility of store queries → Reload interesting results



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THANKS!!!!



> n s i

