Diagnosis for Primary Immunodeficiency (PID) by accessing available resources in South Africa

Monika Esser
Paediatric Rheumatologist

Immunology Unit, NHLS Tygerberg
Stellenbosch University
South Africa

ICORD

RDSA

The ICORD mission is to improve the welfare of patients with rare diseases and their families world-wide through better knowledge, research, care, information, education and awareness.

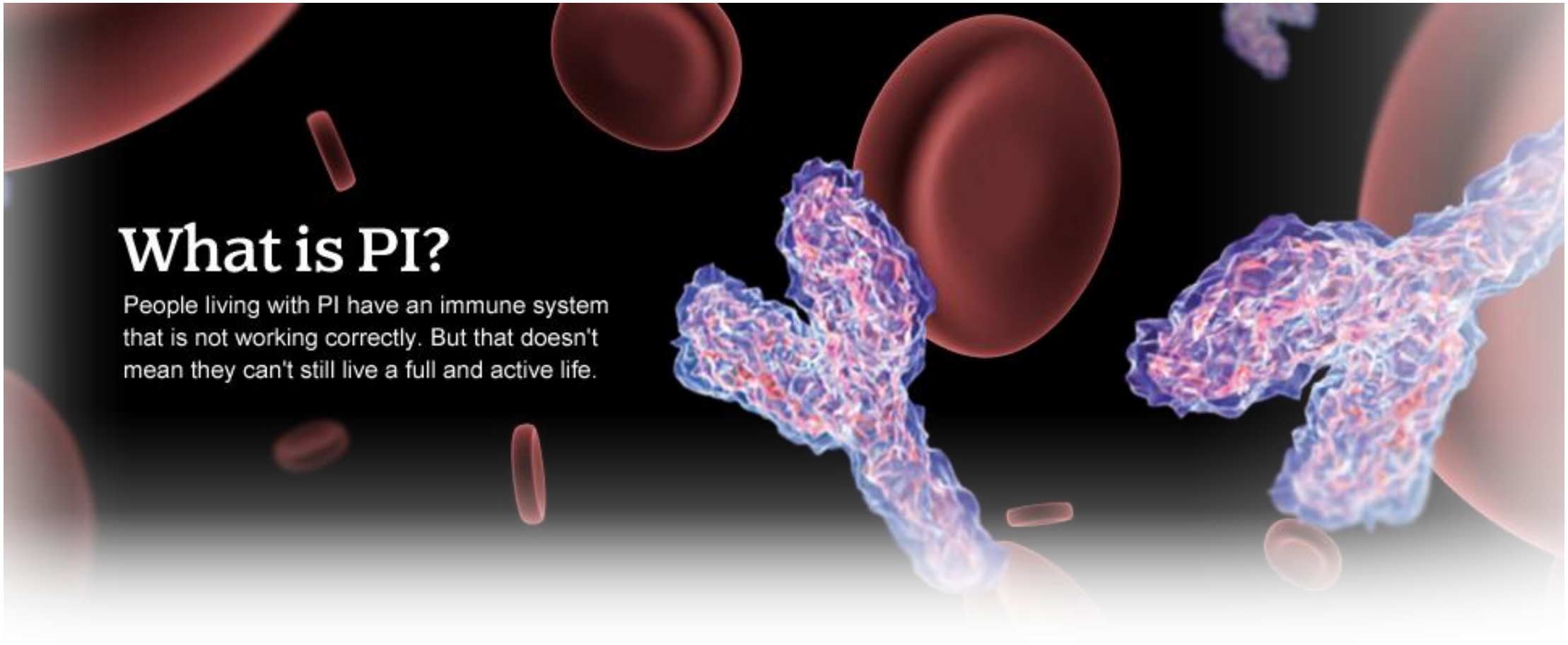
advocacy and engagement between those with ability to prevent, intervene, treat and provide supportive care for patients and families affected by rare diseases living in South

DIAGNOSIS

OVERVIEW

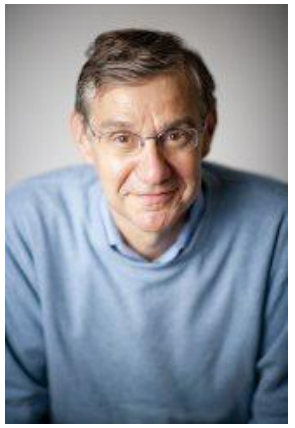
Your aims and mine

- Primary Immunodeficiency (PID) –really rare?
- Value of a diagnosis
- Diagnostic Criteria of PID
- How do/did we diagnose PID ?
- Work of the SA PID Registry
- The “Cost” of essential diagnoses – Cases
- Access to PID genetic diagnosis
- Genetic Molecular capacity in Africa


What is PI?
People living with PI have an immune system that is not working correctly. But that doesn't mean they can't still live a full and active life.

Casanova& Abel
“**PID is NOT RARE**”

SCIENCE VOL 317 3 AUGUST 2007



Inborn errors of immunity are :

NOT just confined to a few rare, familial, monogenic, recessive traits impairing the development or function of one or several leukocyte subsets -
resulting in **multiple, recurrent, opportunistic, and fatal infections in infancy**.

Appears that most individuals :

Each suffer from **at least one of a multitude of primary immunodeficiencies**, the dissection of which is helping to improve human medicine while describing immunity in natura.

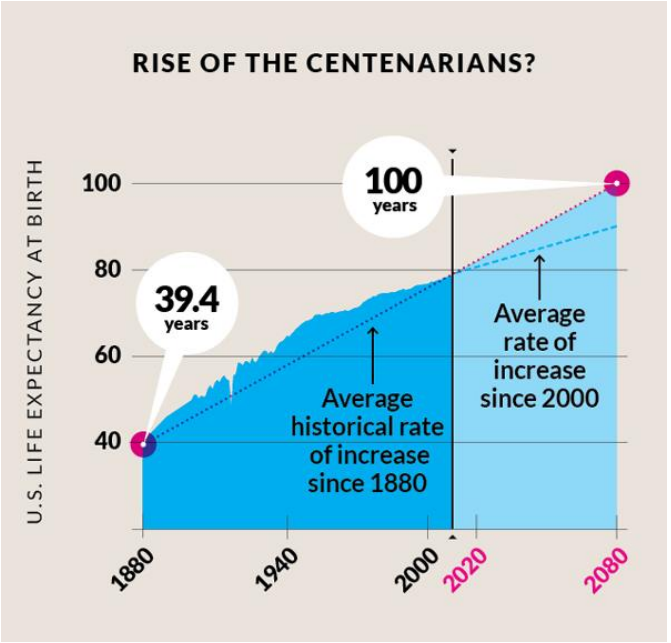
OVERALL : 1 in 1200 livebirths

RARE Diseases – “widely spaced”

- Europe : rare when it affects **1 person per 2000.**
- Depends on the degree of **specificity** used when classifying the different entities/disorders
- **Nearly all genetic diseases are rare diseases**, but not all rare diseases are genetic diseases.
- **Serious, often chronic and progressive**, diseases, over 50% appear during adulthood.
- **No cure for most ?**, but appropriate treatment and medical care can improve quality of life
- Suffer from a **deficit of medical and scientific knowledge** : Difficulties in their quest for a diagnosis
- Science can provide some answers : Hundreds of rare diseases **now diagnosed through a biological sample test**. And knowledge of the natural history of these diseases is improved by the **creation of registries and research networks**

The evolving range of PID as we live longer…

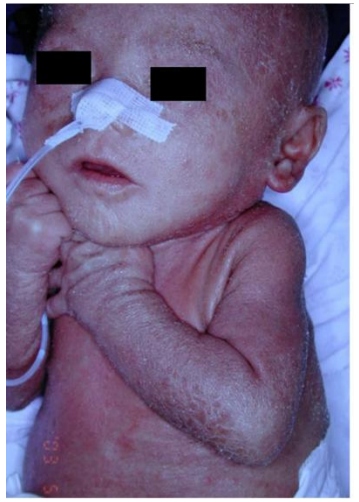
- Nearly 300 monogenic traits
- Single type of infection predisposition also
- Any severe infectious illness potential PID
- Polygenic inheritance patterns



PID Diagnosis masked until times of medical progress !

Discovery of Major Types of PI

- **1922** Neutropenia
- **1926** Ataxia-Telangiectasia
- **1929** Chronic mucocutaneous candidiasis
- **1937** Wiskott-(Aldrich) syndrome
- **1944** Purification of γ-globulin
- **1950** Lymphocytophthisis (SCID)
- **1952 Agammaglobulinemia (XLA) and treatment with γ-globulin**
  (1993 Identification of Btk as site of mutation in XLA)
- **1953** Alymphocytosis (SCID)
- **1954** Acquired agammaglobulinemia in an adult woman (CVID)
- **1957** Chronic granulomatous disease
- 1957 Swiss-type agammaglobulinemia and lymphopenia (SCID)
- **1968 Bone marrow transplantation for SCID**

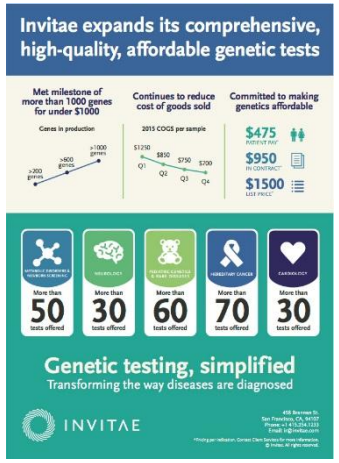


- **1982 Recognition of AIDS**
- **1982 IVIG in the US**
- **1991 Gene therapy** trials for ADA deficiency

Ongoing – GENE PANELS and new PID genes

“Invitae Announces Major Expansion of Its Test Menu for Neurological, Pediatric, and Rare Genetic Conditions and Introduces New Panels for Inherited Metabolic Disorders and Newborn Screening Confirmation “

(Company achieves mid-year goal of more than 1,000 genes in production)

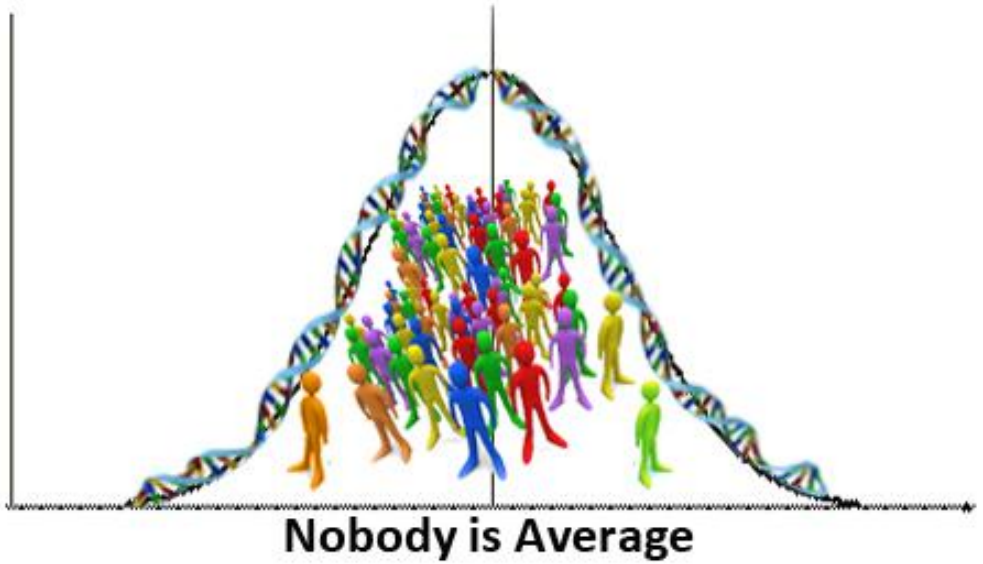


Evolving IUIS Classification (2014)

- predominant **antibody** deficiencies,
- **combined** T-cell and B-cell immunodeficiencies,
- other well defined immunodeficiency **syndromes**,
- congenital defects of number and/or function of **phagocytes**,
- **complemen**t deficiencies,
- defects of immune dysregulation,
- autoinflammatory disorders,
- defects in innate immunity
- Phenocopies

ASSISTED by
ESID Clinical Diagnostic Criteria 2016

Who will **NOT** develop PID ?



Diagnosis

Diagnostics : The art or practice of medical diagnosis

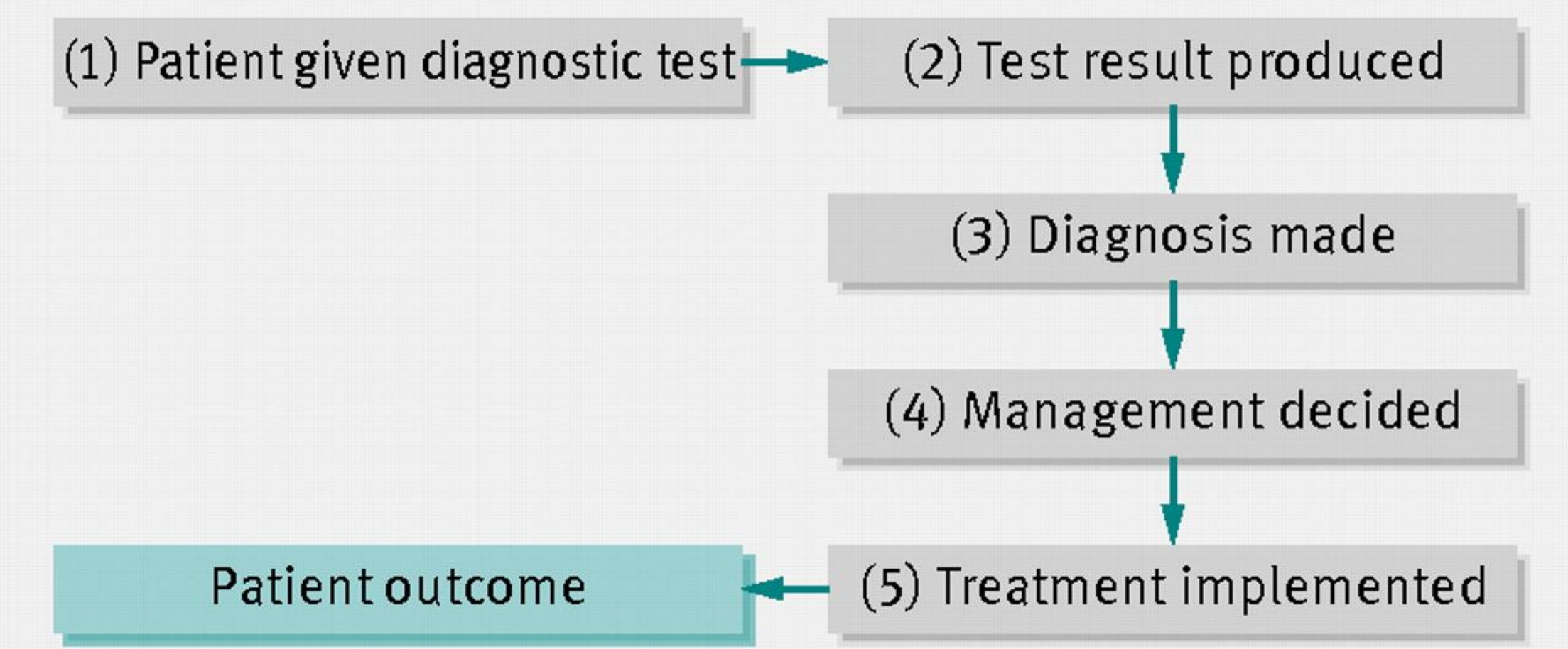
- **Symptom** or a distinguishing **feature** serving as supporting evidence in a diagnosis.
- An **instrument or a technique** used in medical diagnosis.

Value of Diagnostic

- “The value of a diagnostic test is not simply measured by its accuracy, but depends on **how it affects patient health**”
- Improvements in test accuracy will not benefit patients unless they lead to **changes in diagnoses and patient management**

- Improved decision making is only one route by which tests affect patient health - empirical evaluations are needed to compare the effect of test strategies on patient health

Bottom line of diagnosis



Symptom diagnostic JMF WARNING SIGNS

Modified for South Africa

+

BCG dissemination

Recurrent TB

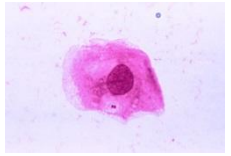
Meningococcal Infection

“Local”Warning signs for primary immunodeficiency (Modified Modell)

- Eight (6) or more new ear infections within 1 year.
- Two or more serious sinus infections within 1 year.
- Two or more months on antibiotics with little effect.
- **Two or more pneumonias within 1 year.**
- Failure of an infant to gain weight or grow normally.
- **Recurrent, deep skin or organ abscesses.**
- Persistent thrush in mouth or elsewhere on skin, after age 1.
- Need for intravenous antibiotics to clear infections.
- **Two or more deep-seated infections.**
- **Parasitoses (e.g. PJP and Giardia).**
- Auto-immune manifestations, especially in the very young.
- **A family history of Primary Immunodeficiency (or unexplained early death).**

And

- **BCG Dissemination**
- **AND Recurrent Meningococcal Infections**
- **Recurrent tuberculosis**



Strongest Predictors for PID

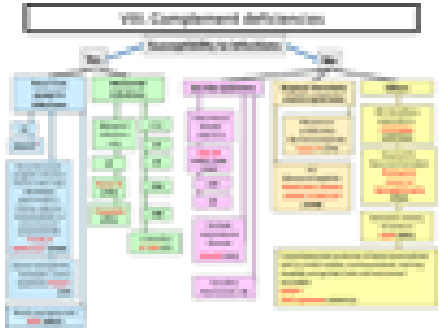
- **Family History** – the most important predictor of PID

- **Use of IV antibiotics** for sepsis and
  failing to thrive for neutrophil and T cell related disorders

- **Hypocalcemia** with or without seizures,
  congenital heart defects (mainly conotruncal anomalies),
  absence of thymic shadow on CXR,
  delayed umbilical cord detachment (>30 days)

CLINICAL ALGORITHM DIAGNOSIS

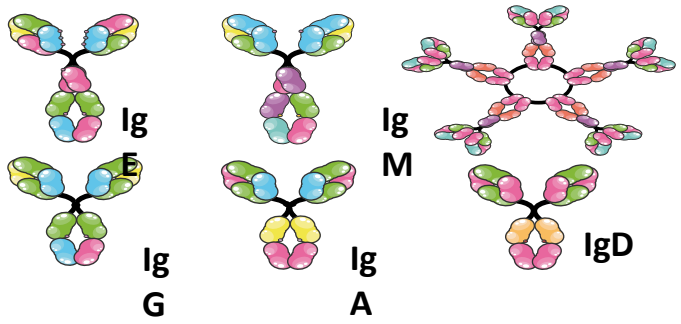
Bousfiiha, Journal of Clin Imm 2013, 33(6)1078-1087



OR : Step wise laboratory testing - STAGE 1 TESTING

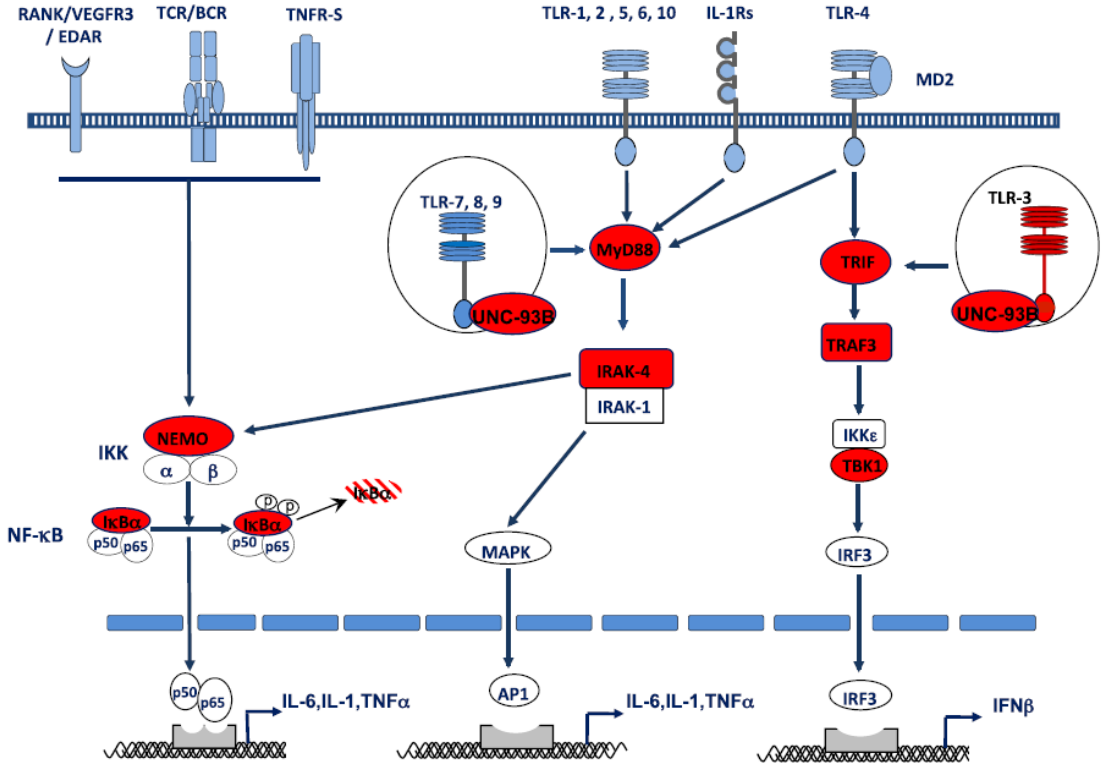
Test for **HIV**, CMV, EBV, TB where relevant
FBC & differential count : **Number of PN (<500/mm3)**
Lymphocytes < 1500
CRP & ESR
Signature organisms eg BCG, PCP, Meningococcus
Screen for Cystic Fibrosis where indicated **(**SWEAT TEST)

Quantitative Immunoglobulins: IgG, M, A & E or **globulin fraction.**

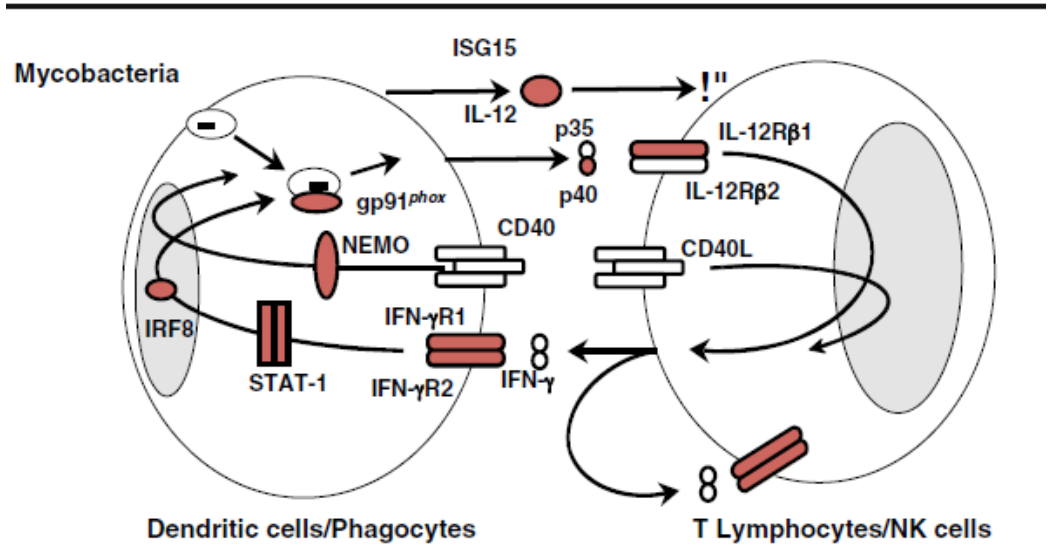


IgG value of less than 3 g/L (300 mg/dL) – Cheap Rule Out

And some have **this testing** available (?)



Genetic defects of TLR/IL-1R signaling pathways (eg Herpes Simplex Encephalitis)



MSMD: MSMD-causing gene products in the IL-12/23-IFN-γ circuit. (eg Mendelian susceptibility to TB)

PIDs : Diagnostic Procedure

- **Clinical phenotype, physical examination**
- **Origin, family history**

- **STAGE 1 Testing**
- **Immunophenotyping**
- **Functional assays (+/- specific of the suspected PID)**

- **Genetic diagnosis**

South African Registry Data

Universities of Stellenbosch, Cape Town and Witwatersrand

Faculty of Health Sciences,
University of Stellenbosch

NATIONAL HEALTH LABORATORY SERVICE

UNIVERSITY OF CAPE TOWN
IYUNIVESITHI YASEKAPA • UNIVERSITEIT VAN KAAPSTAD

"A national registry for PID helps to describe the locally reported spectrum of genetic immune deficiency diseases.
In that way, it addresses the clinical care needs of patients, the services needed, the monitoring requirements of treatment,
training requirements and also locally relevant research questions.
The added benefit is the creation of awareness; the ultimate aim is to improve the care of PID patients."

SA PID Registry
SOUTH AFRICAN PRIMARY IMMUNODEFICIENCY REGISTRY
E-mail: rina@sun.ac.za

S A PRIMARY IMMUNODEFICIENCY REGISTER

Referring Centre

1. Institution:
2. Referring doctor : Dr _____
3. Address: _____
4. **Contact No :** Phone : _____ Fax : _____ e-mail : _____

Patient ID

5. Hospital No: _____

6. **Surname :** _____
7. **First Name :** _____

8. **Birth date** d d m m y y y y (00 = UNKNOWN EG. 00/00/1989)
9. **Sex :** M F (99 = unknown)

10. **Age at diagnosis (age last birthday) in months** (99 = unknown)

11. **Ethnic group** Black White Coloured Asian Other (specify)

12. **Residential address (past 6 months)** Street _____ Suburb _____ Town _____ Province _____ Tel nr. _____ Postal Code _____

13. **Health centre (clinic/day hospital) nearest to residence** _____

DISEASE

14. **Diagnosis** _____ Family hist of PID: YES/NO

15. **Dominant infections** _____ Ig replacement YES/NO

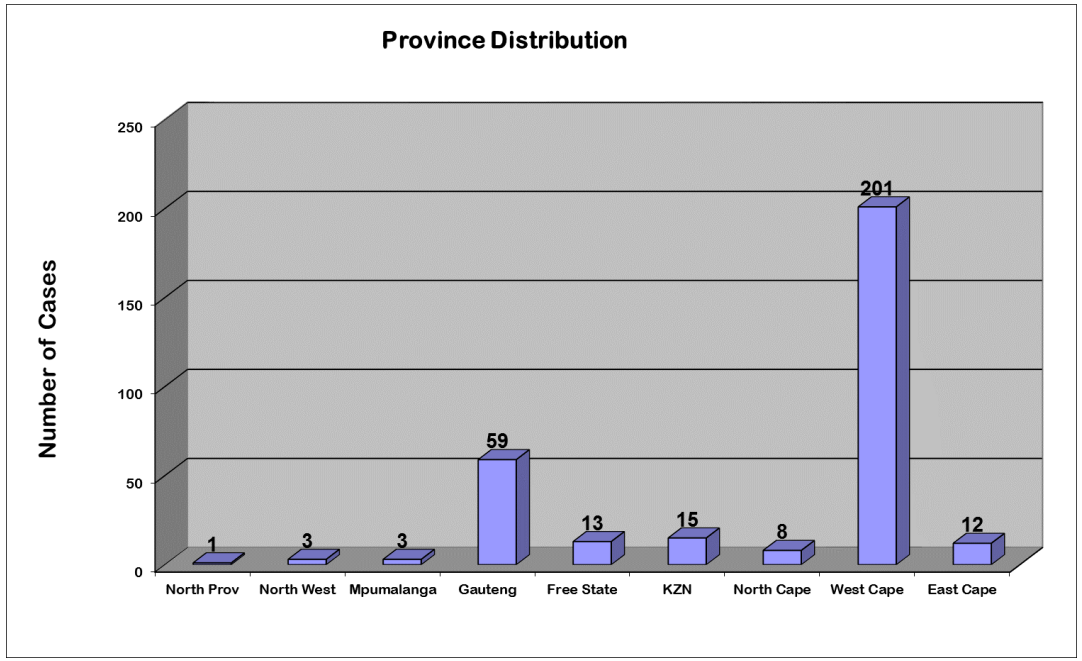
16. **Date of diagnosis** d d m m y y y y

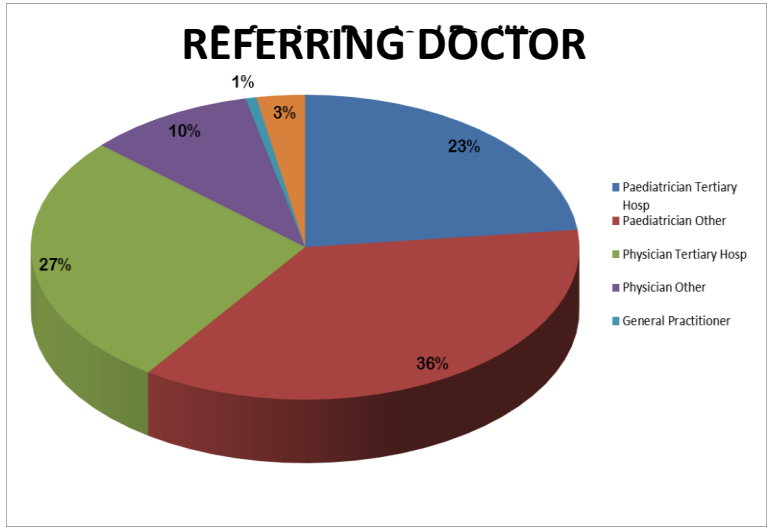
17. **Most valid basis of diagnosis** Clinical Immunological Molecular

18. **Date last contact** d d m m y y y y

19. **Immunology Testing**

- WBC
- Lymph
- Neutro
- Eosino
- Hb
- Platelets
- ESR
- CRP
- CD_3
- CD_4
- CD_8
- CD_{19}
- CD_{16} & $_{56}$
- Neutrophil Burst/ NBT
- PHA
- Con A
- Prot A
- Pokeweed
- Candida
- IgG
- IgM
- IgA
- IgE
- Ab testing: Pneumo
- Tetanus
- Total comp
- Deficient comp
- Molecular Ax
- Haemophilus
- Pertussis
- Diptheria



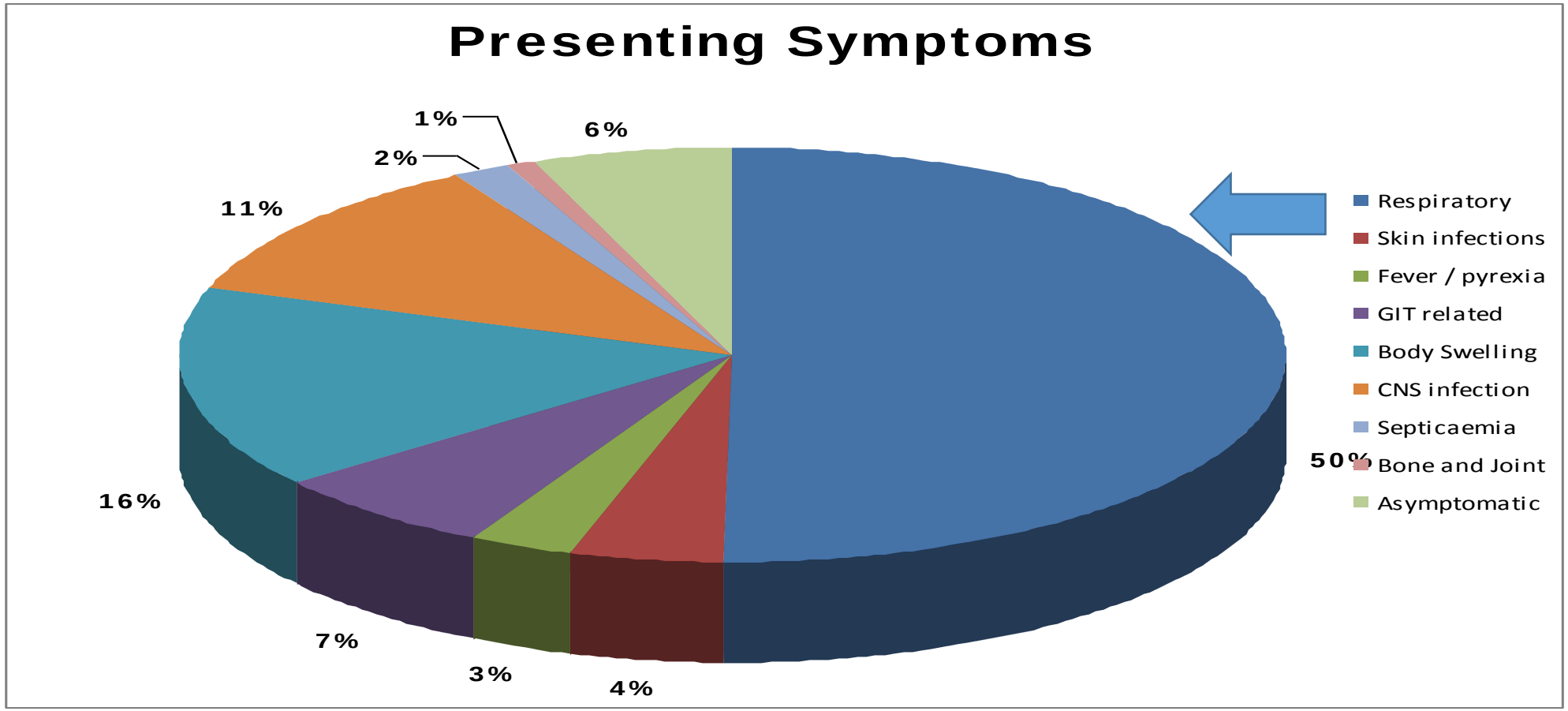


SA PID Registry
SOUTH AFRICAN PRIMARY IMMUNODEFICIENCY REGISTRY
E-mail: rina@sun.ac.za

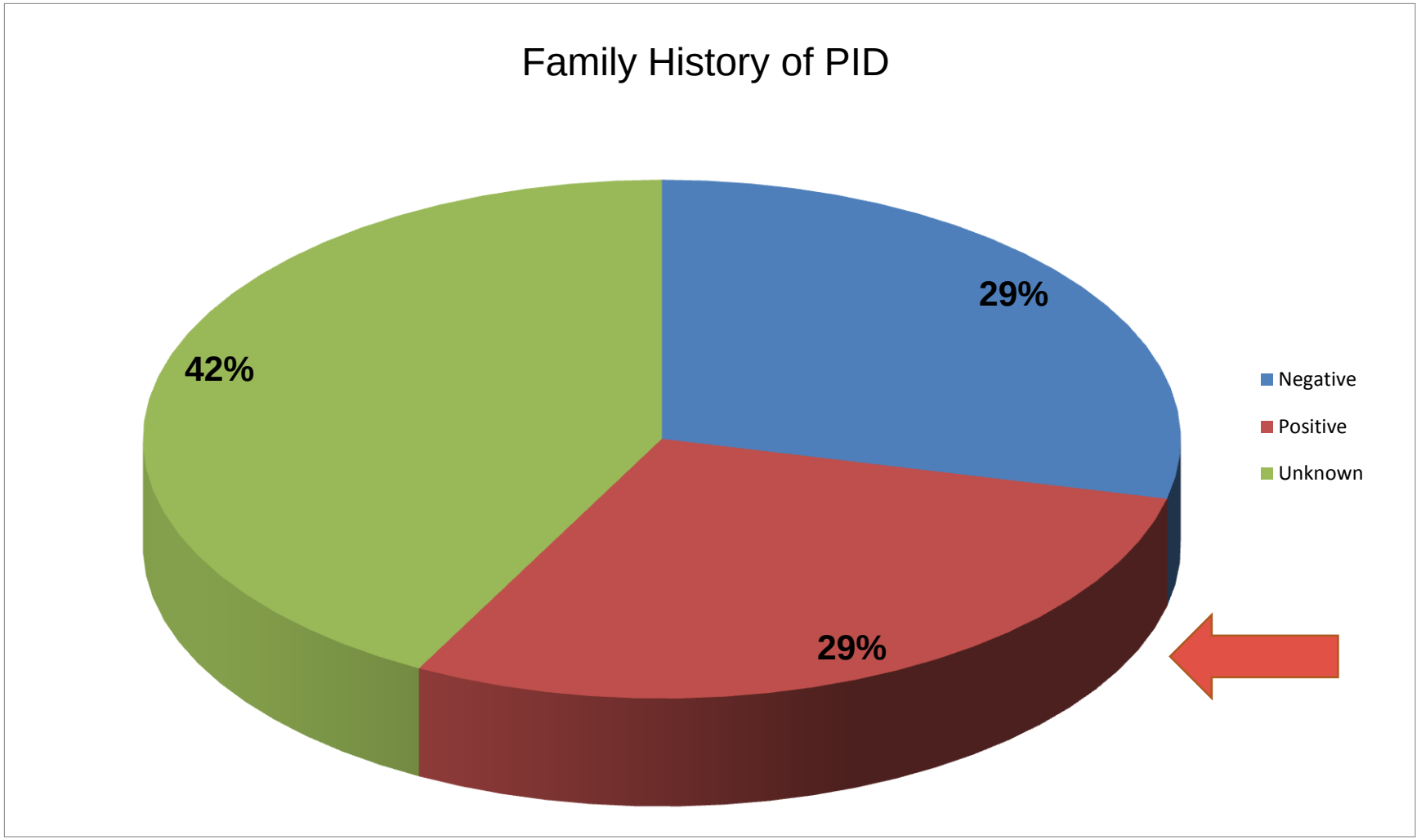
SA PiD Registry

SOUTH AFRICAN PRIMARY IMMUNODEFICIENCY REGISTRY

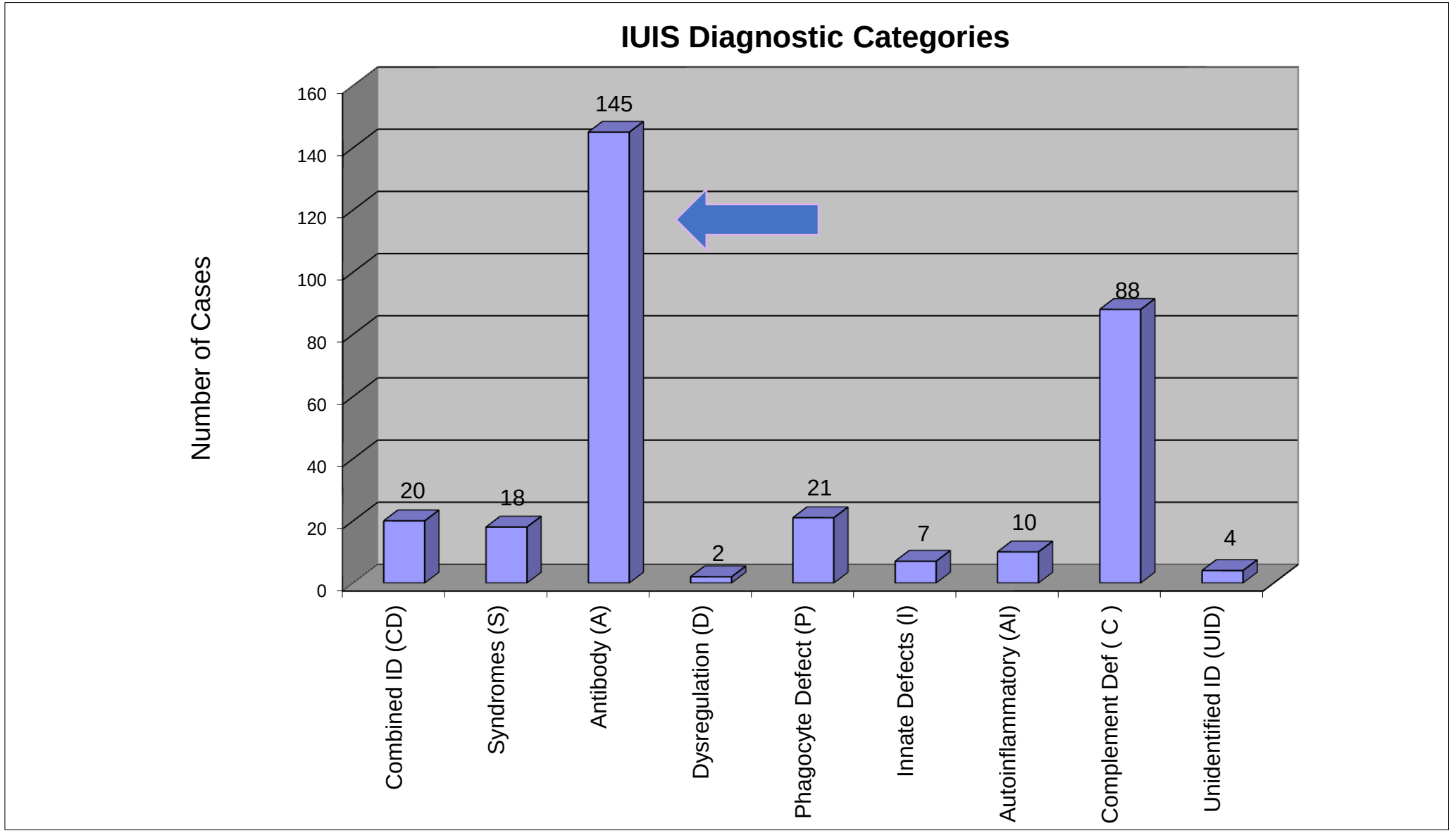
E-mail: rina@sun.ac.za



Clue to PID - **History**



315 Patients recorded of 5800 min expected



SA PID Registry
SOUTH AFRICAN PRIMARY IMMUNODEFICIENCY REGISTRY
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Local relevance : TB findings

- 281 patients - **15 patients with 28 episodes of TB**
- (3 co-infections with *Mycobacterium avium* (*M. avium))*

- 11 Severe Combined Immunodeficiency (SCID) - 5 known episodes of BCG dissemination
- 7 MSMD suspected or confirmed/ very likely (2 NEMO def excluded)
- Mycobacterial infections - 2 patients with Agammaglobulinaemia,
- - 2 patients with CVID
  - 2 NEMO deficiency (1 and 3 episodes of TB episodes respectively)
- - 1 patient with Interferonopathy – MDR, Spinal TB
- - 1 persistent CNS BCGosis – PID –novel mutation MAP3K

Diagnostic PID Test Cost

TEST CODE	TEST NAME	PROCEDURE CODE	PRICE
ANTIBODY (HUMORAL) DEFECTS			
FBC	Full Blood Count + Diff	3797, 3755	191.40
IMM	IgG, IgA, IgM	4182	372.90
IGE	IgE	4513	186.40
SUBG	IgG subclasses	4106	1200.40
SECA	Secretory IgA	3948	194.30
IMMDEF	Lymphocyte subsets (B-cell, T-cell and Nk-cell numbers)	3816	1439.00
SPAB	S.pneumonia antibodies	3948	194.30
HINF	H.influenzae antibodies	3948	194.30
TET	Tetanus antibodies	3948	194.30
DIP	Diphtheria antibodies	3948	194.30
BF	B-cell function	3978	775.40
BMEM	Memory B cells	3816	863.40
BTK	Brutons Tyrosine Kinase	3816	863.40
CD40L	CD 40 Ligand	3816	1151.20
T-CELL DEFECTS			
HIV	HIV Antibodies (Screen)	3932	192.20
HIVPCR	HIV PCR	3974	1125.20
FBC	Full Blood Count + Diff	3797, 3755	191.40
IMMDEF	Lymphocyte subsets (B-cell, T-cell and Nk-cell numbers)	3816	1439.00
TMEM (> 6 yrs)	Recent Thymic Emigrants Naive/ Memory/ Helpers	3816	2302.40
NAIVE (< 6 yrs)	Recent Thymic Emigtants Naive Helpers	3816	863.40
TCELLR	Alpha beta/ gamma delta T cells	3816	863.40
CGC	Common Gamma Chain	3816	863.40
TH17	TH 17 Cells	3816	1151.20
FOXP3	T Regulator Cells	3816	1151.20
LYMPHOCYTE PROLIFERATION TESTS TO MITOGENS			
PHAPR	PHA	3978	775.40
PMAPR	PMA	3978	775.40
PMAIPR	PMA + Ionomycin	3978	775.40
CD3PR	Anti CD3	3978	775.40
IL2PR	Anti CD3 + IL-2	3978	775.40
CONPR	CON A	3978	775.40
PWMPR	PWM	3978	775.40
LYMPHOCYTE PROLIFERATION TESTS TO RECALL ANTIGENS			
VZVPR	Varicella zoster	3978	775.40
CANPR	Candida	3978	775.40
TETAPR	Tetanus	3978	775.40
NEUTROPHIL DEFECTS			
FBC	Full Blood Count + Diff	3797, 3755	191.40
NEUTF	Neutrophil functions (Burst phagocytosis chemotaxis)	3950, 3952	2551.00

BASIC PID SCREEN:

FBC&Diff – R 200.00
IgG,M,A - R 373.00
HIV Elisa - R 200.00

TOTAL : < R 800.00

Cost of conventional diagnostic investigation $ vs "yield" of diagnosis

Simple…… diagnoses

Combined ID

- "Typical" SCID — R 600.00 (43 US $)
- **With Syndromes**
- Hyper IgE – "classical" — R 200.00 (14$ US)

Antibody related

- Agammaglobulinaemia
- (Transient) Hypogammaglobulinaemia — R 400.00 (29 US $)
- IgA – true symptomatic deficiency

Phagocyte

- Persistent Neutropaenia
- Classical Chronic Granulomatous Disease — R 200.00 (– R2500)

Complement

- C5/C6 Complement deficiencies
- HAE Type I

But Diagnostic Cost $$$$$$$ - if not so simple……..

- Hypomorphic/leaky SCID
- Evolving Syndromic features
- Hypogammaglobulinaemias
- Prolonged transient HGG
- CGD
- Dysregulations
- Autoinflammatory
- Phenocopies

THE COST OF GENOMICS……?

4 Pillars of PID Diagnosis – **which Shoe Fits** ?

History

Examination

Stage 1 laboratory (and extended Immune phenotyping)

Genetics

Genetic Diagnosis
Orphanet Directory of diagnostic tests

Intended to help professionals to obtain :

a) timely and

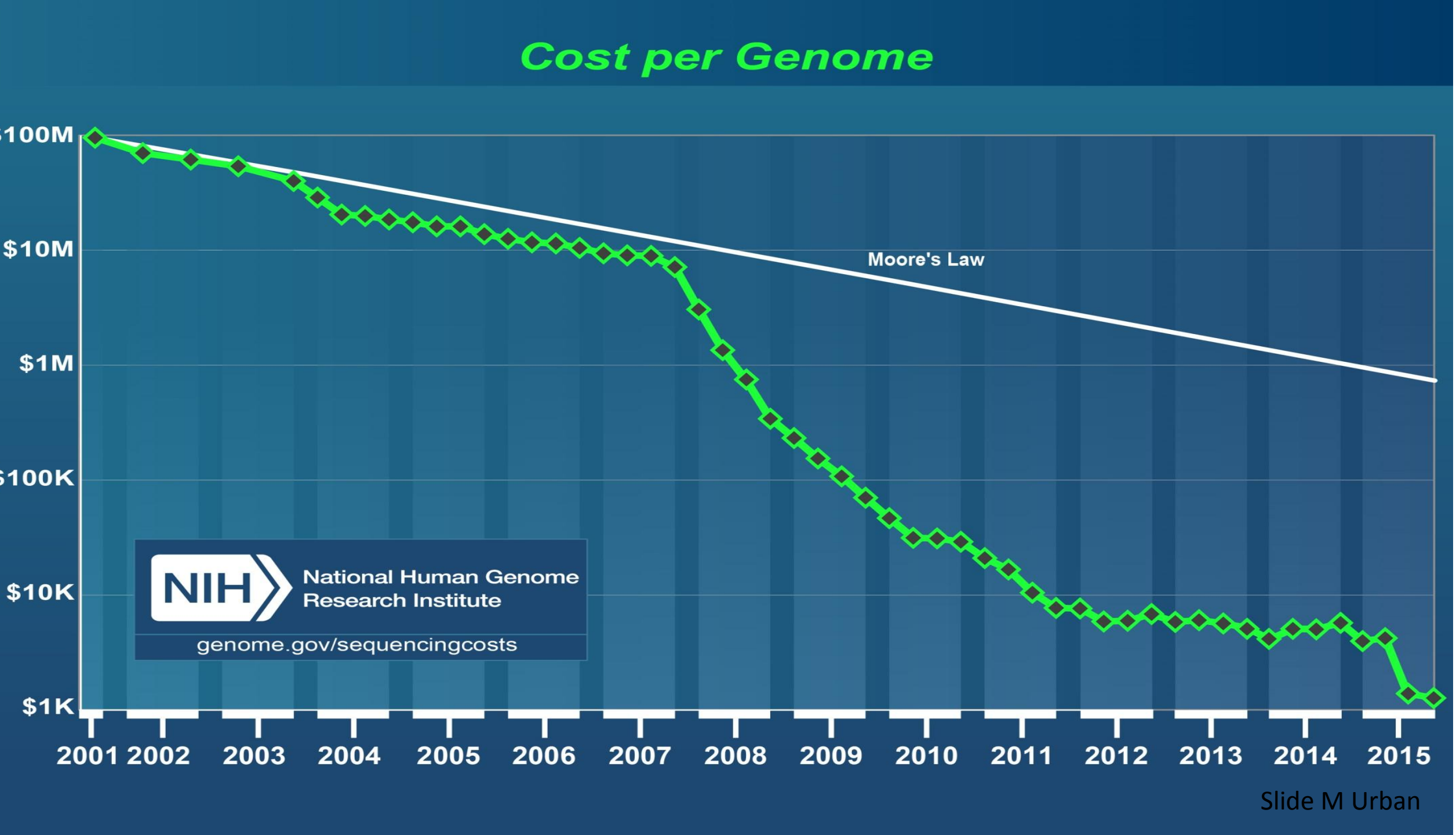
b) accurate diagnosis for patients affected by a rare disease

(“Data Collection and update of diagnostic tests” procedure, soon available)

Diagnostic test in Orphanet is tagged:

a) one technical procedure of 3 levels i) Speciality: main method cat. (eg Mol Gen)

ii) Objective : goal of test (eg Target Mut)
iii) Technique : spec. technology (eg Sanger)



Slide M Urban

Implications for clinical genetic testing

Limitations as a diagnostic test:

- High ‘analytical specificity’
- Often low ‘clinical sensitivity’

→ Phenotype-based approach to diagnosis of PIDs:

- Genetic testing only available, or useful, in certain instances

Slide M Urban

Phenotype-based approach is limited

- Only a minority of monogenic disorders have been addressed by these methods
- Many genetic disorders don’t have unique phenotypes
- **Genetic heterogeneity:**
  - Individuals with similar phenotypes may results from a mutation in any one of many genes
- Multifactorial disorders:
  - Person’s phenotype has multiple genetic (and enviromental and epigenetic) contributions

COST – versus VALUE of ESSENTIAL DIAGNOSIS

Because tests can affect patient health by :

- changing treatment decisions
- affecting time to treatment
- modifying patient perceptions and behaviour

Example
The Newborn Screening (NBS) for PID

- **TRECS** (T cell receptor excision circles) **&** **KRECS** (Kappa-deleting recombination excision circles)
- Analysis of **SCID screening** results in over 3 million infants from 11 programs of population-based NBS with the TREC : Fifty-two cases of SCID and leaky SCID/Omenn syndrome , incidence of **1 in 58,000 births**
- Goal of NBS : **detect treatable disorders** that are threatening to life or long-term health before they become symptomatic, ie PID
- **SCID only one of several (PIDs)** presenting early in life. Not completely sensitive, but NBS test for SCID able to identify some other PID with profound reduction of naïve T cells e.g. **complete DiGeorge syndrome, leaky SCID, ataxia telangiectasia but also in Prematurity**.
- Awareness of **genetic heterogeneity**, (i.e. the situation when a single phenotype could be caused by any one of multiple alleles or non-allelic different locus mutations)
- “Poor man’s alternative” : **CD3 T cell count of ≤1500 cells/microL and** absence of naïve T cells (oligoclonality)

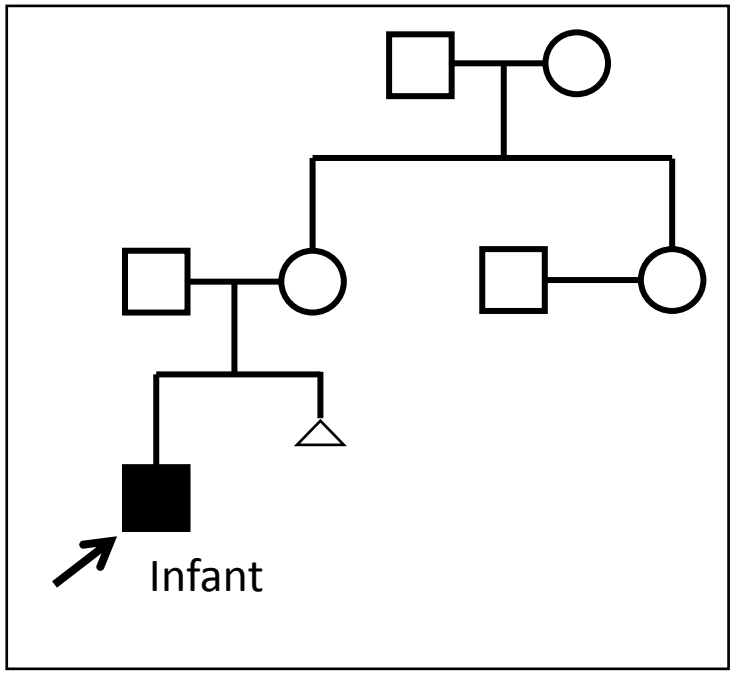
Case

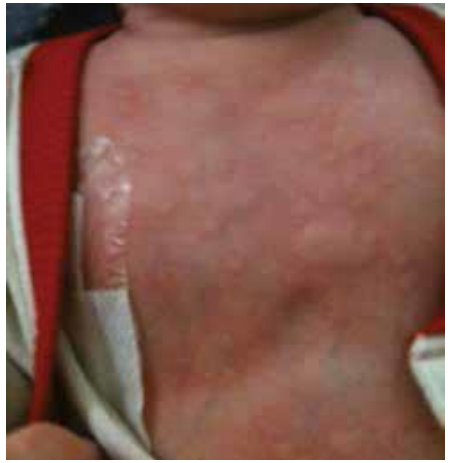
EMERGENCY

Male infant

Evolution over many months…

- Recurrent infections
- Intractable diarrhoea
- Eczematous rash
- Multiple auto-antibodies





Astute clinician suspects IPEX syndrome

- **I**mmune dysregulation
- **P**olyendocrinopathy
- **E**nteropathy
- **X**-linked recessive

IPEX : requires urgent BMT !

C. Gray, Curr Allergy and Clinical Immunology 2014

Result:	Hemizygous mutation identified
Mutation details:	Gene : *FOXP3* Location : Exon 12 DNA Description : c.1157G>A Protein Description : p.Arg386His (p.R386H) Consequence : Missense

Interpretation

[redacted] is hemizygous for a previously reported *FOXP3* missense mutation, p.R386H (Tsuda *et al* 2010 J Autoimmun 35:265-268). This mutation is predicted to be pathogenic and the result confirms a diagnosis of IPEX syndrome.

→ Urgent result allowed for successful stem cell transplant

SIMPLE SEARCH

ipex *
(*) mandatory field

- (•) Disease name
- ( ) Gene name or symbol
- ( ) OMIM
- ( ) ICD-10
- ( ) Orpha number

→ OK

OTHER SEARCH OPTION(S)

> Alphabetical list

: : Immune dysregulation-polyendocrinopathy-enteropathy-X-linked syndrome

Orpha number	:	ORPHA37042	ICD-10	:	E31.0
Synonym(s)	:	Autoimmune enteropathy type 1 IPEX	ICD-O	:	-
			OMIM	:	304790 [↗]
Prevalence	:	<1 / 1 000 000	UMLS	:	-
Inheritance	:	X-linked recessive	MeSH	:	-
Age of onset	:	Infancy Neonatal	MedDRA	:	-

SUMMARY

Immunodysregulation - polyendocrinopathy - enteropathy - X-linked (IPEX) syndrome is a severe congenital systemic autoimmune disease characterized by refractory diarrhea, endocrinopathies, cutaneous involvement, and infections.

Prevalence is unknown. Less than 150 cases have been reported to date but the disease has probably been underestimated.

IPEX syndrome usually develops during the first few days or weeks of life and affects exclusively boys. It manifests with the sequential appearance of the triad of enteropathy, autoimmune disease, and cutaneous involvement, but the clinical features and severity of the disease can vary considerably between individuals. Severe autoimmune enteropathy manifests with intractable secretory diarrhea leading to malabsorption, electrolyte disturbance and failure to thrive. Vomiting, ileus, gastritis or colitis can also be observed. Patients also present with autoimmune endocrinopathies, generally insulin-dependent diabetes mellitus (type 1 DM), but also thryroiditis leading to hypothyroidism or hyperthyroidism. Skin involvement consists of a generalized pruriginous eruption resembling eczema, psoriasis, and/or atopic or exfoliative dermatitis. Less frequently,

Additional information

Further information on this disease

> Classification(s) (4)
> Gene(s) (1)
> Other website(s) (2)

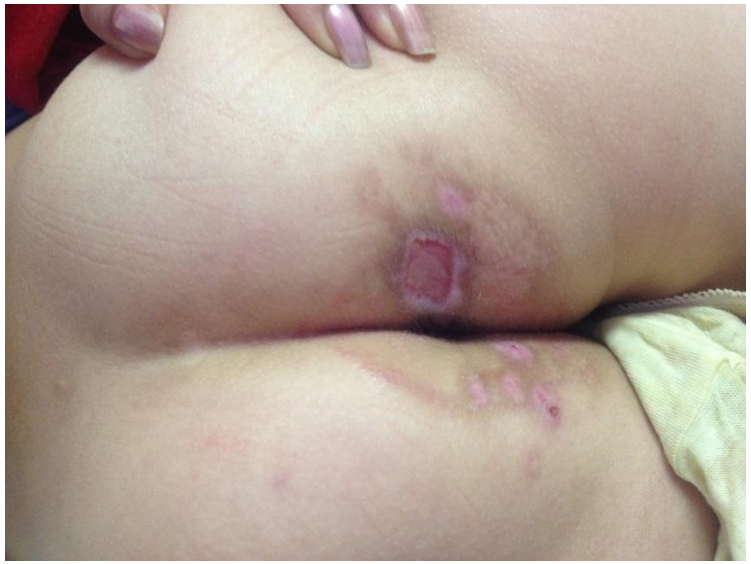
Health care resources for this disease

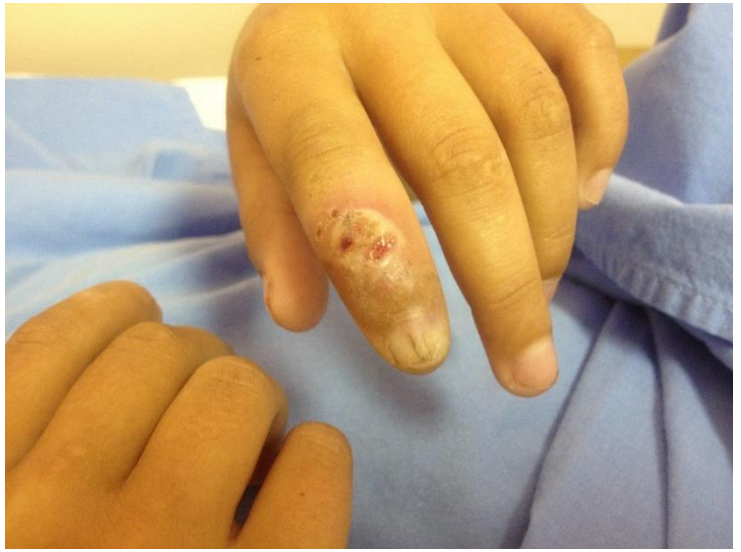
> Expert centres (197)
> Diagnostic tests (19)
> Patient organisations (33)
> Orphan drug(s) (0)

Research activities on this disease

Case of mistaken “ neglected child”

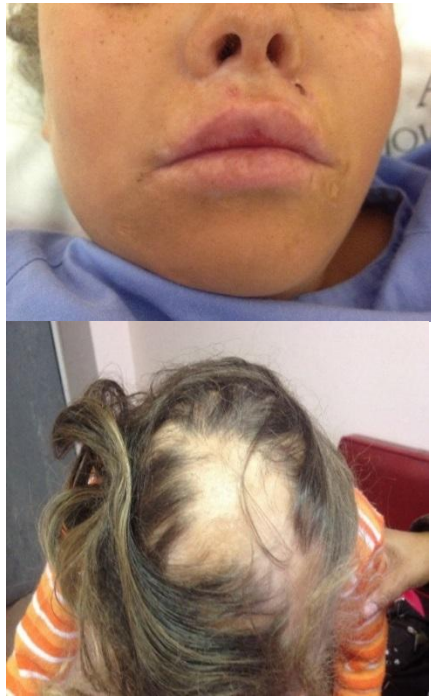
Severely underweight, late onset severe bacterial, viral, fungal infections …gradual onset vitiligo, enteropathy, encephalopathy





LRBA Deficiency CVID

(common variable immunodeficiency variant) on exome sequencing



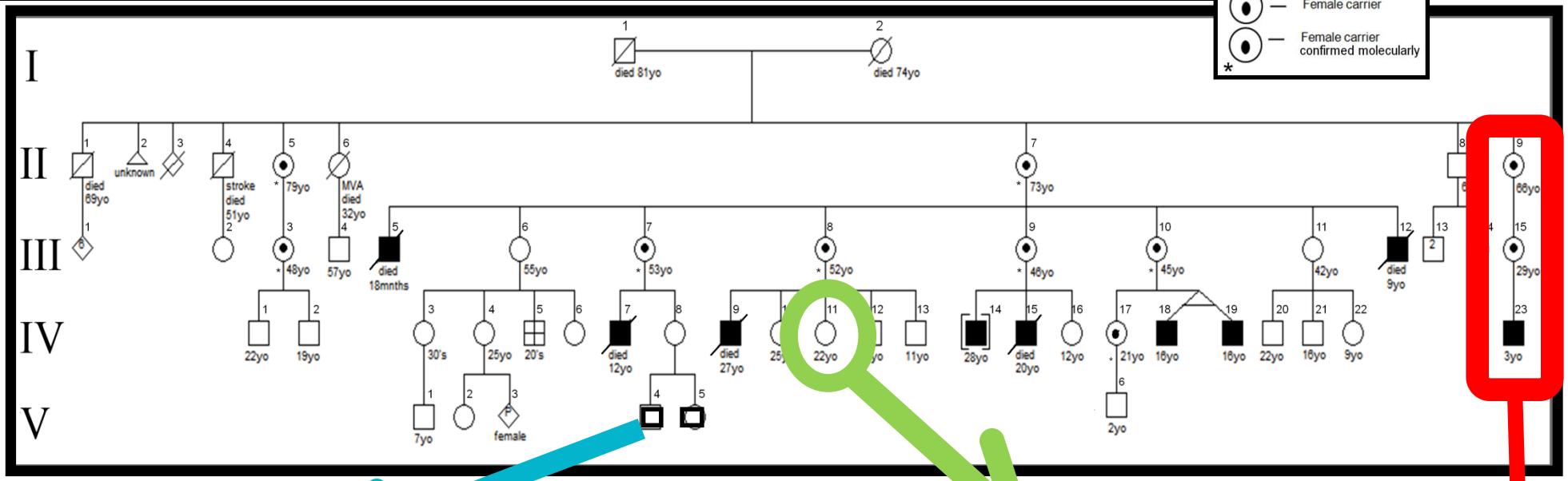
LRBA : Lipopolysaccharide (LPS)-responsive beige-like anchor (LRBA)- novel gene essential for normal function of the immune system (vesicle trafficking).

Eighth CVID gene, mutation of which causes **CVID and autoimmunity**, and is associated with **inflammation**.

Treatment potential – but too late in this case

CASE Counselling

A family with agammaglobulinaemia



WHY Do They Die ?

(HEPATITIS early Adulthood)

- "Poor " SES
- All lived in one house
- Back yard Wendy houses
- 1 toilet inside house
- Bucket toilets

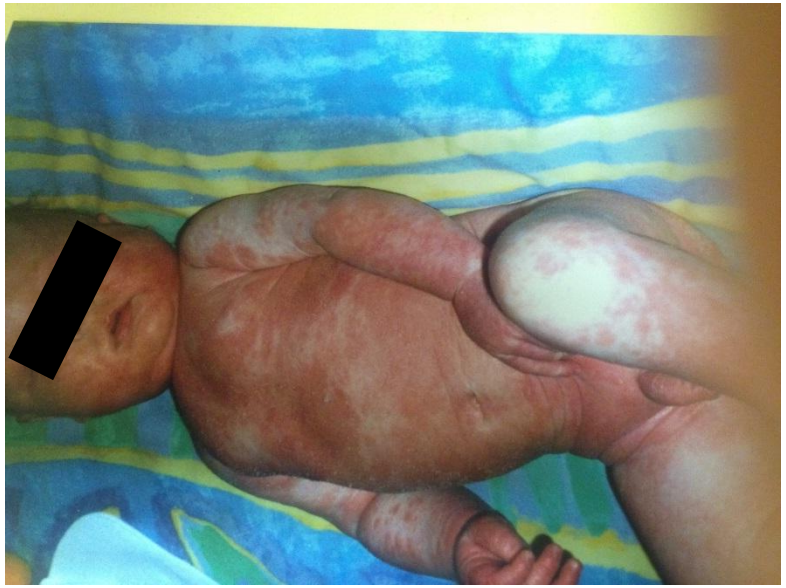
- Adopted as baby
- Middle class family
- At 31 years now :
  - Employed
  - Healthy
  - Good quality of life

Mother: Not accepted diagnosis

(Slide M Urban)

Case

Severe Infections but **normal immune tests** !



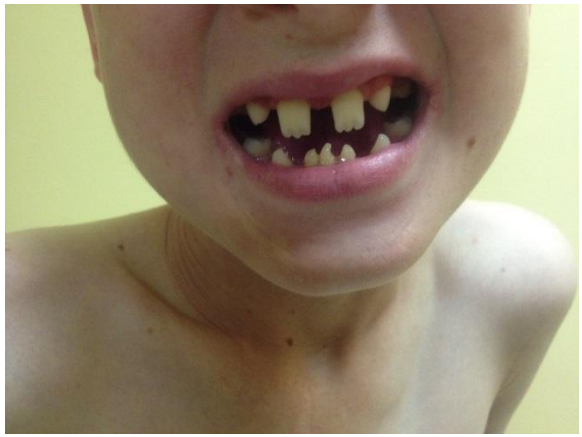
Neonatal
Erythroderma

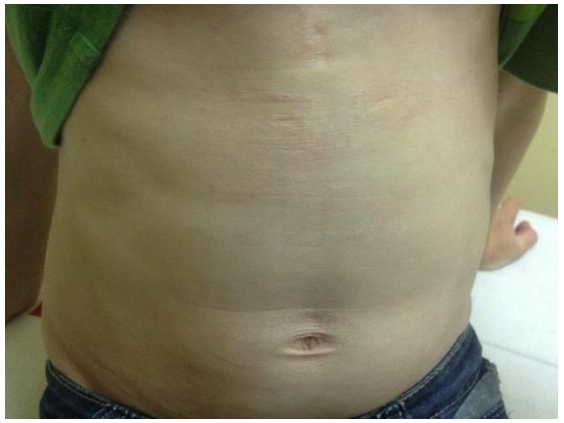
Infancy
Septic Pericariditis

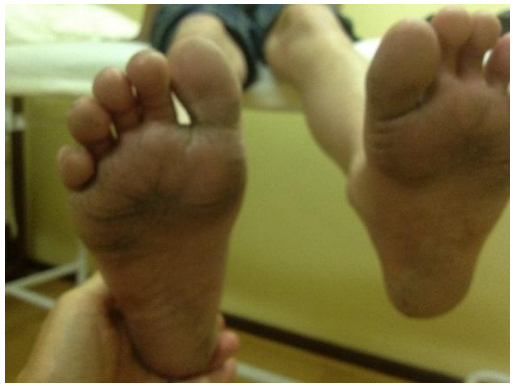
Young Boy
Tuberculosis

Teenager
M.*Avium* arthritis

Later Ectodermal Dysplasia







NEMO deficiency

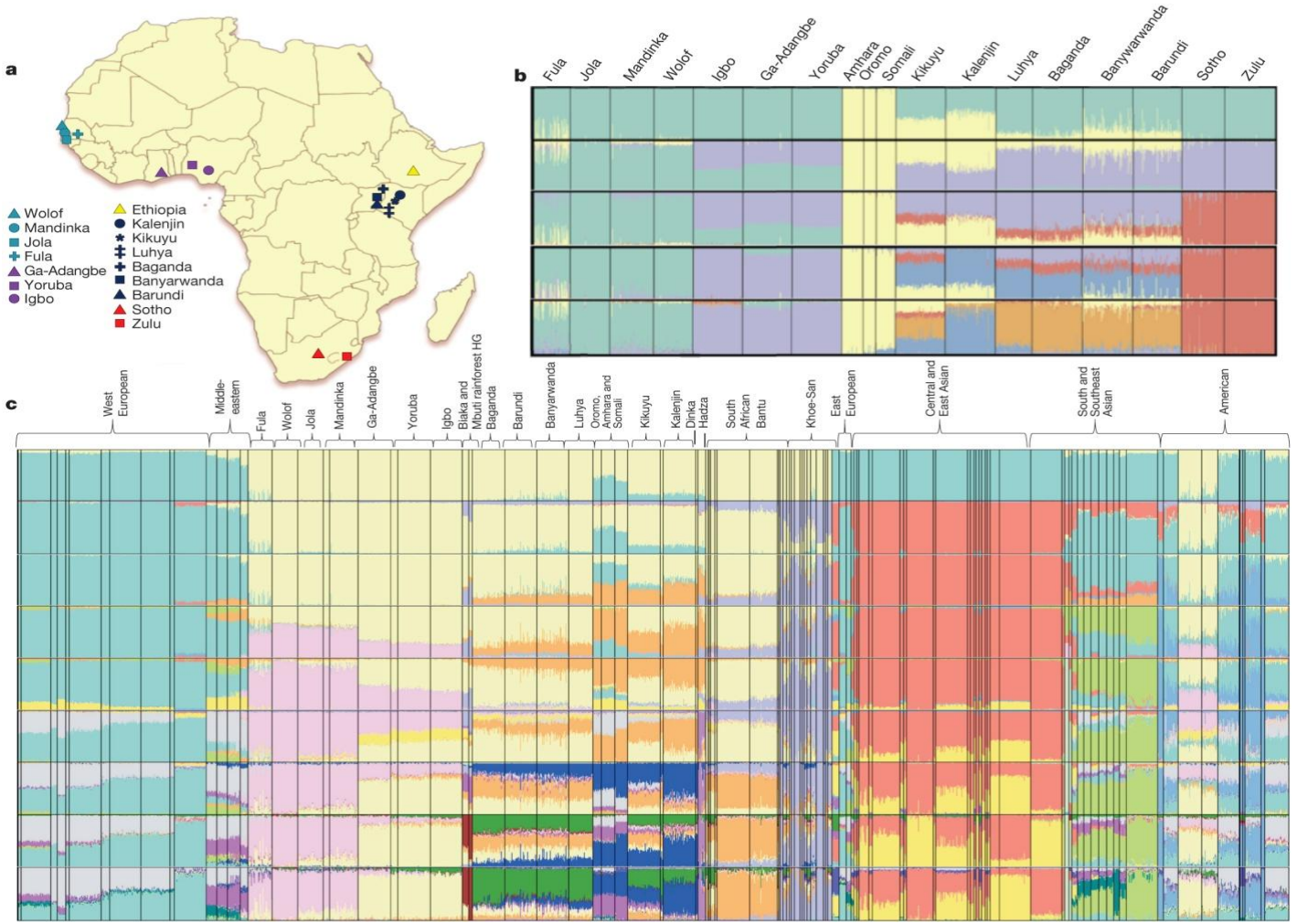
Nuclear factor-kappa B essential modulator/ Inhibitor of Kappa B Kinase gamma (IKK gamma) protein is required for the activation of the NF-kappa B family of transcription factors, regulate gene expression and the development of a number of organ systems, including the **immune system, alerting to any type of infection.**

Need for access and feasibility of molecular diagnosis

- **Confirmation** of defined clinical phenotype
- Where overt PID **immunophenotype is lacking**
- Diagnosis for PID **phenotype diversity**
- Diagnosis for PID **“non classical”** eg. involvement of non-hematopoietic cells such as in ectodermal dysplasia ID with uncertain immune mechanisms causing recurrent infections
- Diagnosis not only of **“public”** genes – non-redundant -required for protective immunity to multiple microbes but also **“private”** genes conferring specific immunity to one pathogen

Cost effectiveness **data analysis** **team discussion**

Public Genes: Populations studied in the AGVP



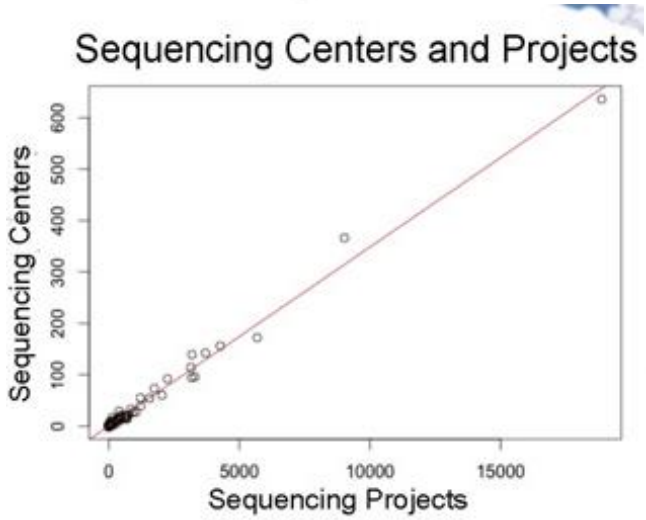
Novel evidence of complex, regionally distinct hunter-gatherer and Eurasian admixture across sub-Saharan Africa.

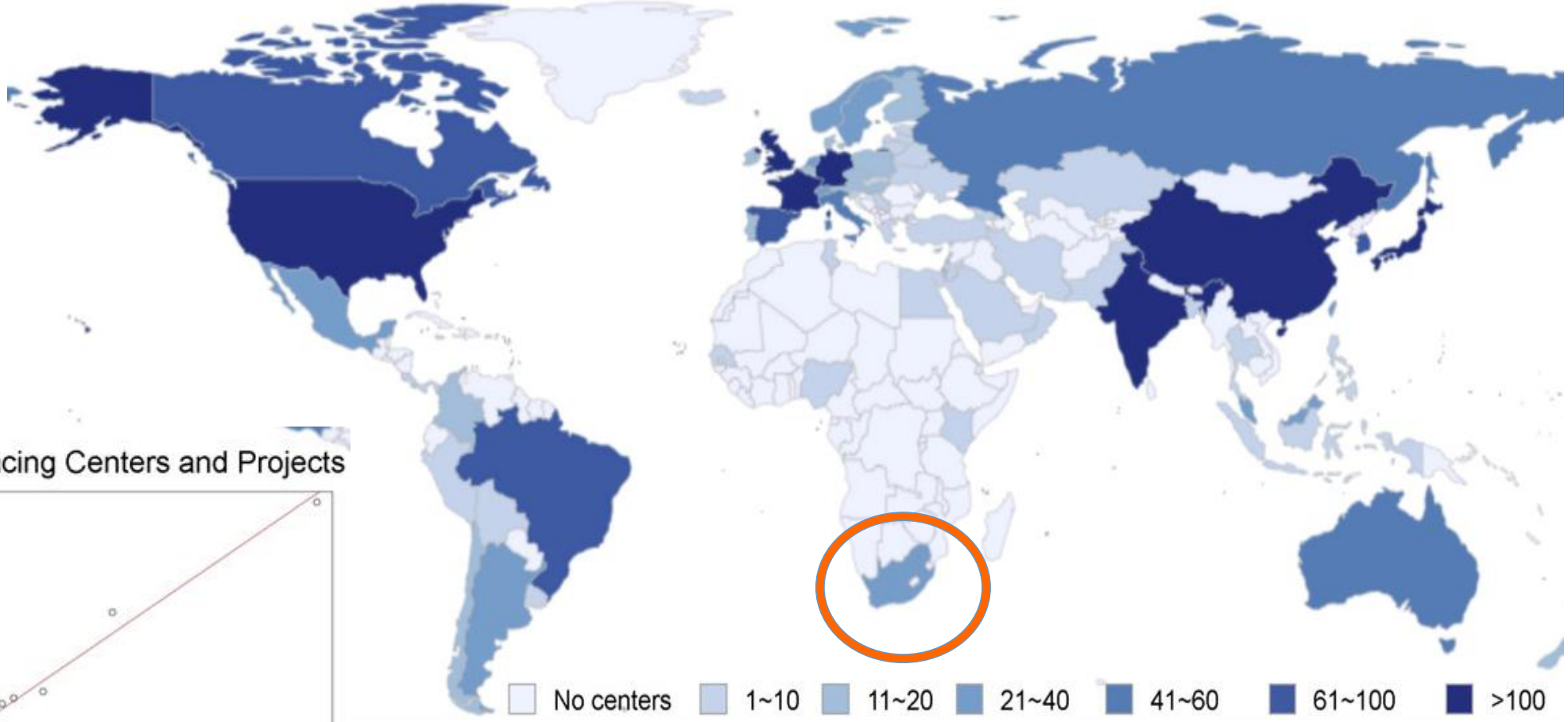
Identified new loci under selection, including loci related to malaria susceptibility and hypertension….

nature

D Gurdasani *et al. Nature* **000**, 1-6 (2014) doi:10.1038/nature13997

Genome sequencing centers per country

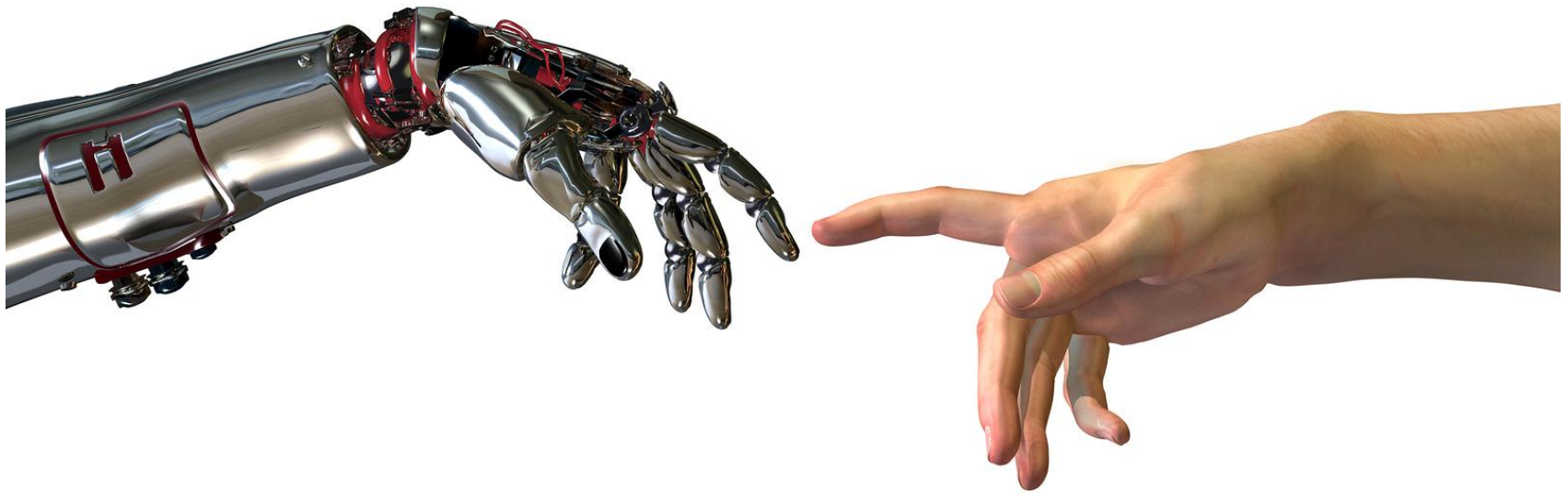




Molecular **Diagnostic** Feasibility in Developing countries

Ready for genomics?

Need for the Collaboration……



Limited resources of genome sequencing in developing countries: Challenges and solutions

Mohamed Helmy et al (Applied & Translational Genomics 9 (2016) 15–19)

“The situation remains unaltered in several regions of the world, especially Africa”

Recommendations:

increasing research funding,

establishing centers of excellences,

encouraging international collaborations and

organizing specialized training programs as possible potential solutions for

Sustainable future improvement of genomic research in developing countries

PIDDGEN

Primary Immunodeficiency Diseases Genetic Network

- AIM : identification of **novel candidate genes for susceptibility to tuberculosis in PID** .
- Scope of Project : to **develop genetic screening tools for PID patients**

NATIONAL HEALTH LABORATORY SERVICE

Faculty of Health Sciences, University of Stellenbosch &
National Health Laboratory Service (NHLS) Tygerberg

TAPER^{TM}DATA – Analysis

- TAPER^{TM} is a seven tier ‘pipeline’ for data filtration (B Glanzmann)
- **Which variants require further assessment ?**

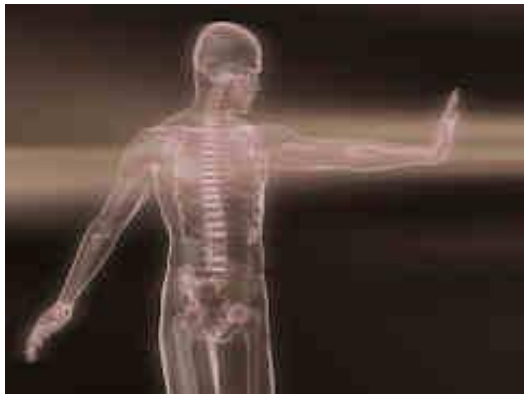
Bioinformatic filtering using TAPER

	Database	Patient
TOTAL GENETIC VARIANTS		22 368
Remove synonymous and non-frameshifts		10 467
Remove normal polymorphisms	1000 genomes 6500 exomes	1 431
Remove if wide interspecies variation	GERP	1 097
Remove if no predicted effect on protein	FATHMM	449
Novel variants		157
Variants with rs numbers		292
Homozygotes		23
Heterozygotes		26

These variants require further assessment

The journey continues

New Frontiers in Immunology

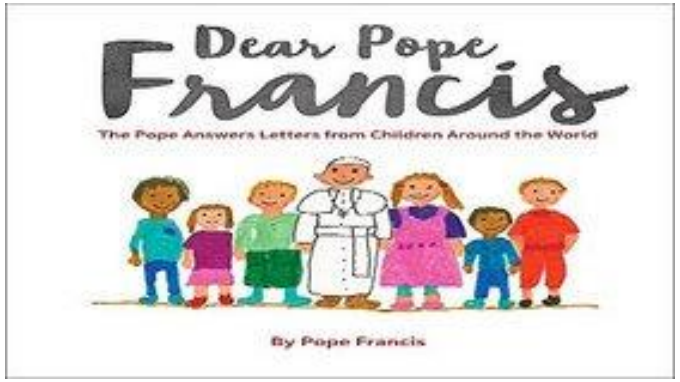


- **clinical genetics, epidemiological genetics, and evolutionary genetics, with the definition of PIDs in this context**, constitutes a new frontier in immunology

- **connect basic research with patient care** From the knowledge gained through this long and enlightening journey through the history of our planet and the evolution of our race, and for the discoveries yet to come the future looks promising.

- **to provide better treatment and in some case even the hope of cure** to our patients. “

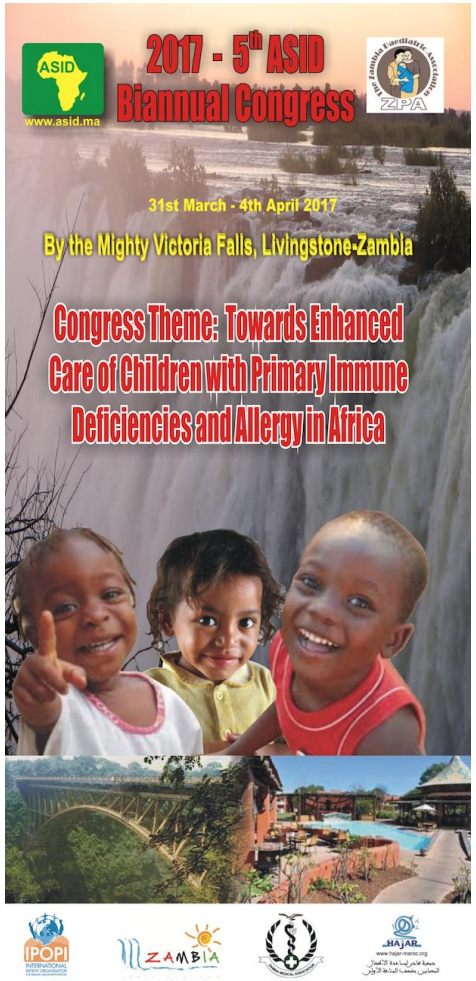
(The Past, Present and Future of Immunology . Austin J Clin Immunol - Volume 1 Issue 1 – 2014)



"These patients, in fact, often are not given enough attention because the idea of profit prevails over the value of human life.

It is fundamentally important to promote greater empathy in society, so that nobody remains indifferent to our neighbour's cry for help, including when he or she is suffering from a rare disease."

Come JOIN us


ASID
www.asid.ma
2017 - 5th ASID
Biannual Congress
ZPA
31st March - 4th April 2017
By the Mighty Victoria Falls, Livingstone-Zambia
Congress Theme: Towards Enhanced
Care of Children with Primary Immune
Deficiencies and Allergy in Africa
IPOPI
ZAMBIA
HAJAR

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- Dr Brigitte Glanzman
- Ms Rina Nortje
- Ms Glenda Durrheim
- Ms Nikola Schlechter

NATIONAL HEALTH LABORATORY SERVICE

SOUTH AFRICAN MEDICAL RESEARCH COUNCIL

MRC SOUTH AFRICA

SA PID Registry

SOUTH AFRICAN PRIMARY IMMUNODEFICIENCY REGISTRY

PIDDSA primary immune deficiency diseases south africa

ALLSA Allergy...or Not? 2016 CONGRESS

Primary Immunodeficiency Workshop

Genetics, Genomics & PID

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- Boyle JM, Buckley RH. Population prevalence of diagnosed primary immunodeficiency diseases in the United States. J Clin Immunol 2007; 27:497.)
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- Mohamed Helmy et al (Applied & Translational Genomics 9 (2016) 15–19)
- The Past, Present and Future of Immunology . Austin J Clin Immunol - Volume 1 Issue 1 – 2014
- J Clin Immunol. 2013 Aug; 33(6): 1078–1087. Published online 2013 May 9. doi

The South African PID Journey and the Future

- David Beatty – dedicated PID service and laboratory at RXH - 1983
- Patrick Bouic - Immunology Laboratory Tygerberg
- Paul Potter – Allergy and Clin Imm Service at GSH
- The South African Bone Marrow Registry -1991, BMT GSH
- Tygerberg – dedicated PID service - 1991
- PiNSA Joy Rosario - 2001 (assistance of IPOPI)
- PIDDSA - 2006
- PID Registry - 2009
- South African Immunology Society Congress -2009
- African Society for Immunodeficiency Diseases -2009
- BMT Gauteng private - 2011
- PID Service Pretoria Academic -2016
- PID Service Albert Luthuli – 2016
- The Future – Collaboration between Industry- Private Enterprise-Universities

H I V