New Challenges in Medical IT

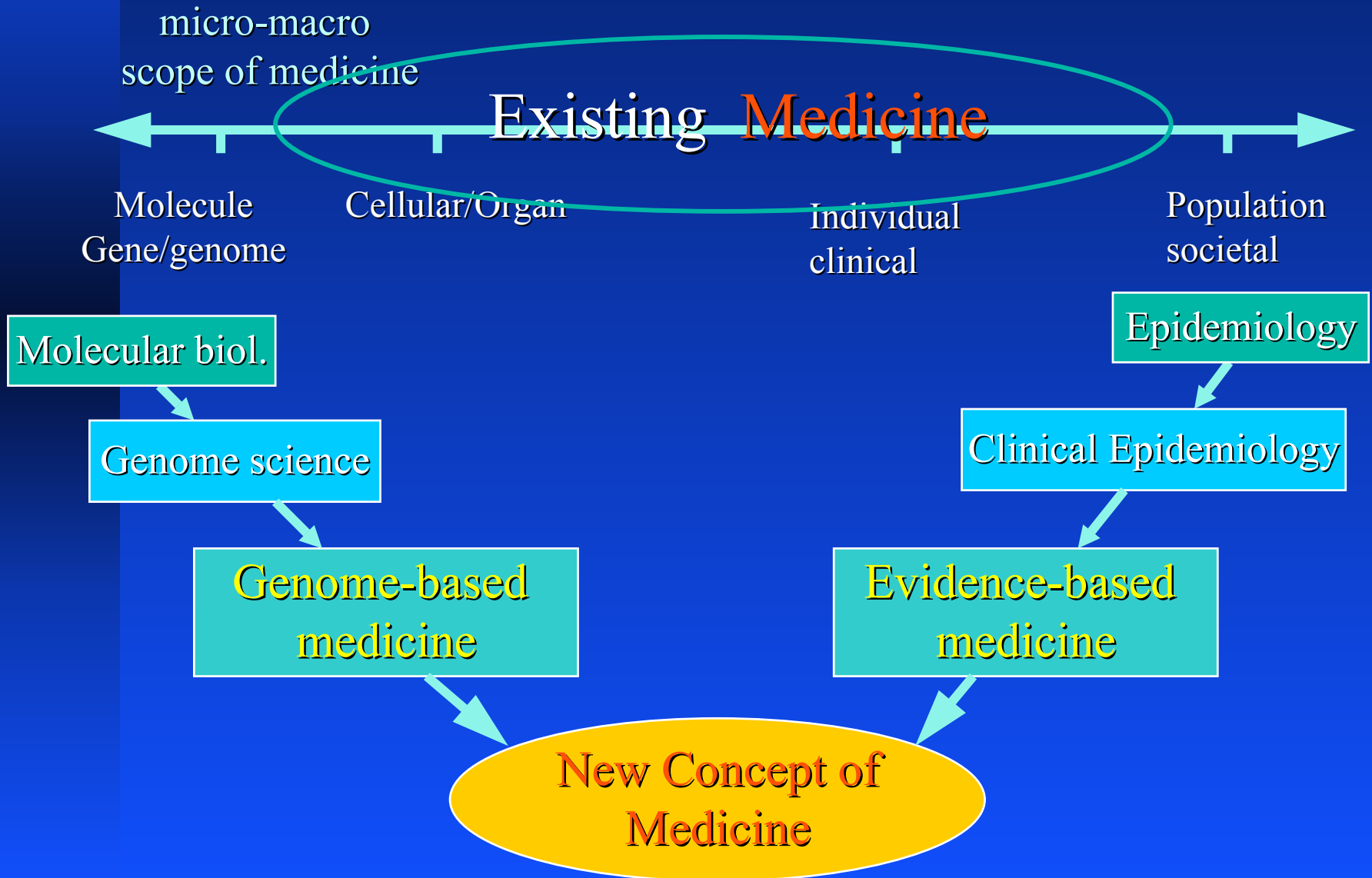
-Computerized EBM and genome-based medicine-

Tokyo Medical and Dental University
Center for Information Medicine
JAMI President Elect
Hiroshi Tanaka

Challenges in Medical IT?

- Target disciplines we should tackle in coming age to extend and deepen our medical informatics field?
- Medical Informatics, Medical IT
  - Start with hospital-based technology primarily to implement clinical system.
  - Now, various medical issues are deeply related with "information", such as, genetic medicine, informed consent, standardization of medicine and so on.
- We are expected to take a major role to bring solutions to all of such issues where medicine and information are closely related.
  - 2nd stage of Medical Informatics/IT
- Various Challenges are there, but we should think about them in relation to questions of what will be the key concept of future medicine.
  - Key paradigm of 21th cent. Medicine

New paradigms of 21th century Medicine



New Concepts of 21th cent. Medicine

"Standardized" Medicine

Homogeneity of high level in "quality of medical care"
Equal opportunity to receive best medical practice

Evidence-based Medicine

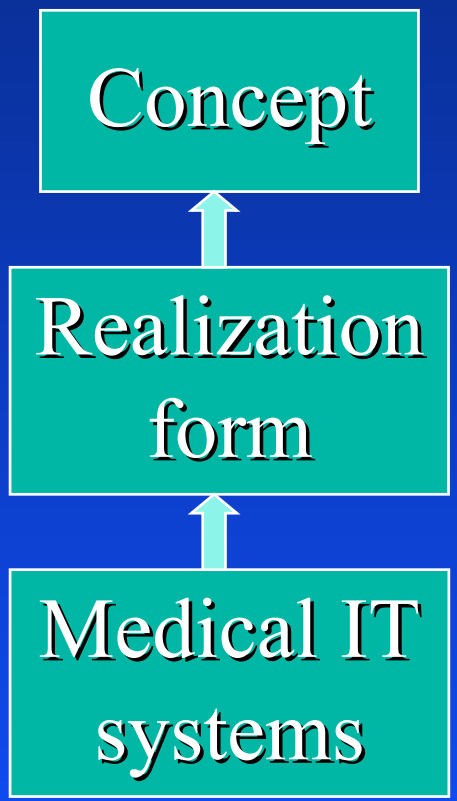
besides

"Personalized" Medicine

Patient-specific care based on genetic polymorphism
Disease susceptibility/
Drug responsibility

Genome-based Medicine

These New Concepts of Medicine Cannot be Realized without Medical IT



Standardized (EB) Medicine
Personalized (GB) Medicine

Evidence-based CPG, Critical path
Genomic Patient Record

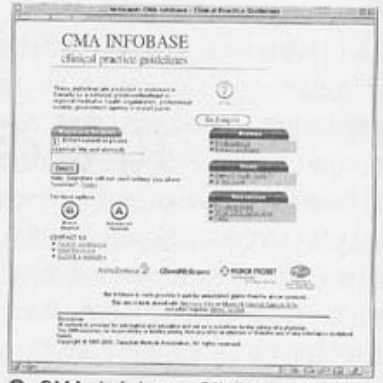
Computerized EB-CPG
Genomic EMR, Genomic DSS

Medical IT for Standardized Medicine

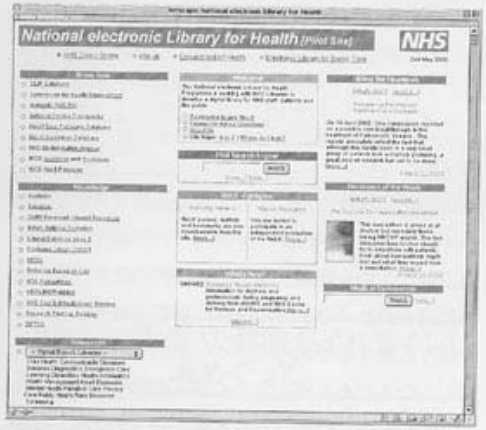
Evidence-based Medicine

- EBM
  - 1991 Gordon Gyatt (Clinical epidemiology)
  - 1993 Sackett(Oxford) **EBM WG**
- "The conscientious, explicit and judicious use of current best evidence in making decision about the care of individual patient" (Sackett)
- Evidences supported by Random clinical trials
- Primary practice of EBM
  - Literature search for evidences of clinical similar situation
- Evidence-based CPG/CP
  - **CPG: Clinical Practice Guideline**
  - **CP: Critical Pathway**

❷ National Guideline Clearinghouse のホームページ

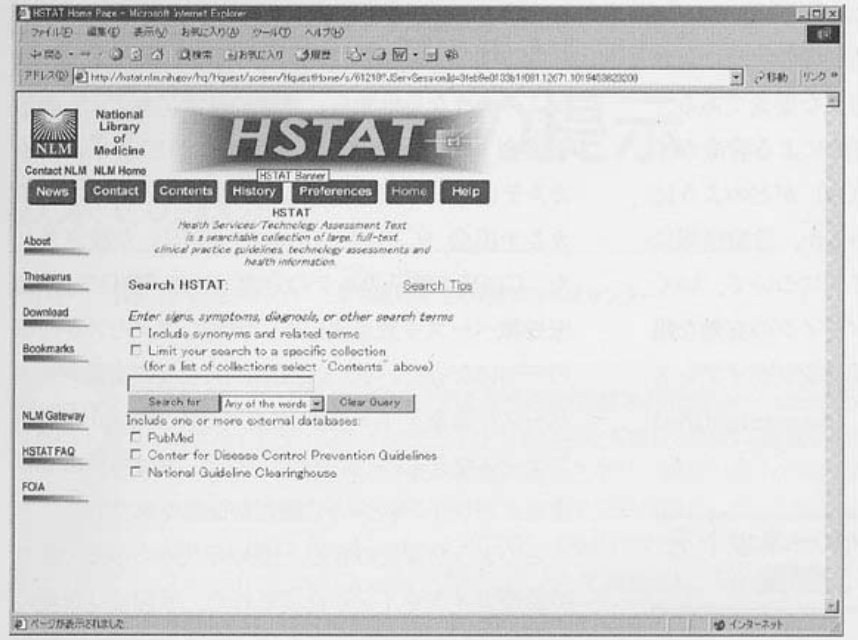


❸ CMA Infobase-Clinical Practice Guidelines のホームページ

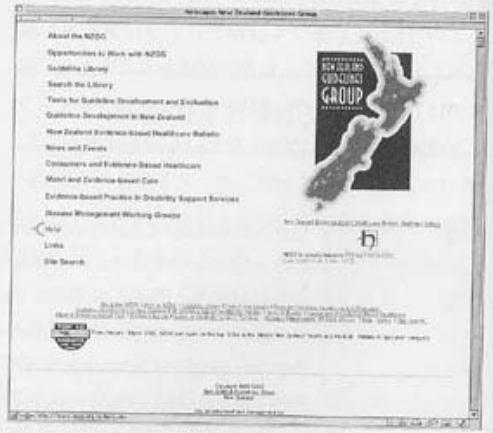


❹ National Electric Library for Health のホームページ

❺ National Institute for Clinical Excellence のホームページ



❻ German Guideline Clearinghouse のホームページ



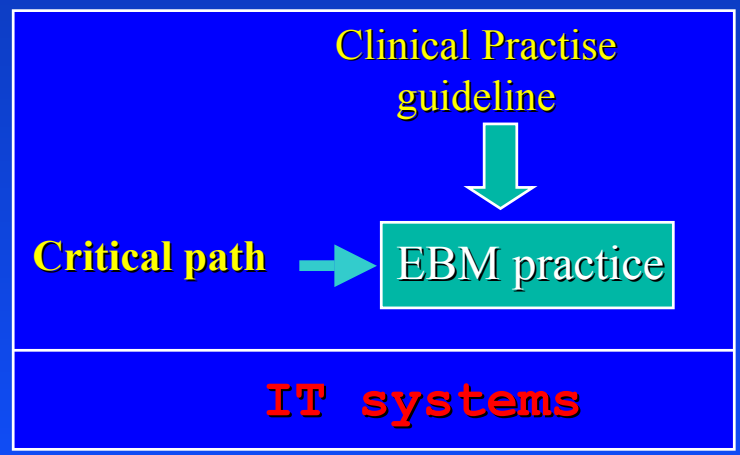
❼ New Zealand Guidelines Group のホームページ

Web-based guideline

IT systems realizing EBM

- Standardized medicine IT
  - Best practice could not be done at the point of care by Primarily EBM
  - So **computerized CPG/CP is needed** to be implemented in physician's information environment

  To attain the Homogeneity at high level in medical care
- Evidence-based computerized CPG/CP
  - Stream of Intelligent DSS instead of expert knowledge
  - Standard terminology and protocol



CPG systems

- To computerize CPG

  It must be machine understandable, able to be used at appropriate situation, it should be triggered automatically when needed

  But we are still lacking in the design concepts

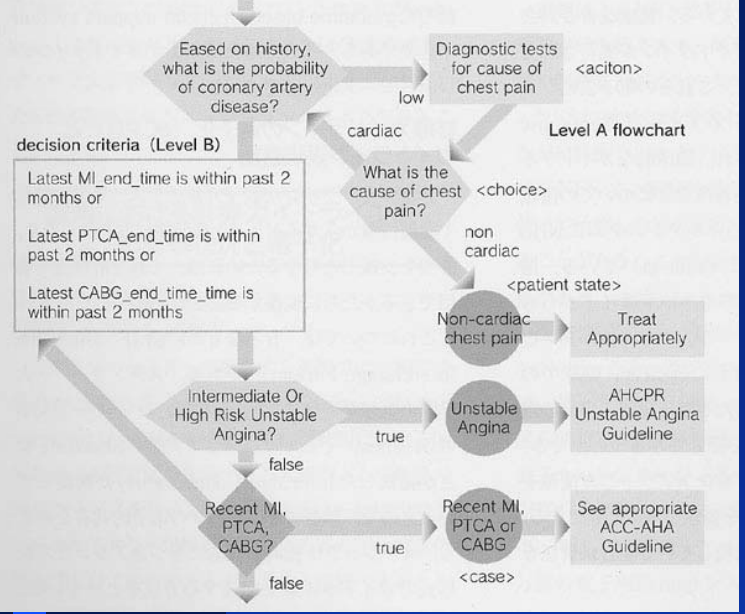
- Example eCPG
  - GLIF (Guideline Interchange Format) Algorithm type、 Intermed Collaboratory
  - GEM (Guideline Element Model) GML

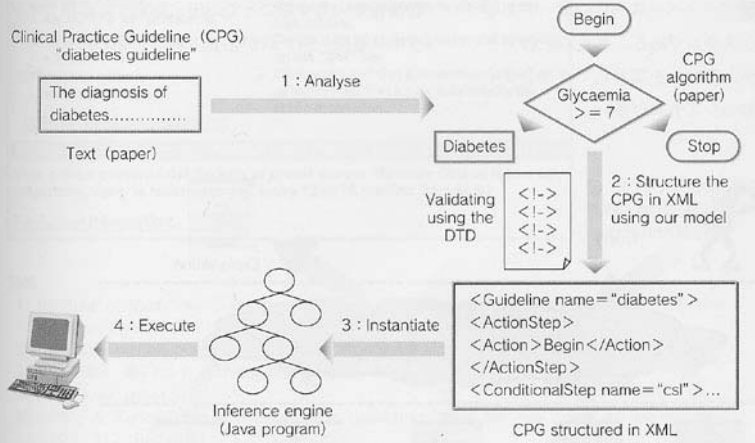
    XML,natural linguage Markup
  - PRO*format*
    - Action,Enqury,Decision,Plan
- **CPG-based DSS**
  - EON blood pressure manage　ATHENA DSS
  - EsPeRproject　breast cancer management OncoDoc　ASTI(drug)

It should be developed together with information modelling of medical practise

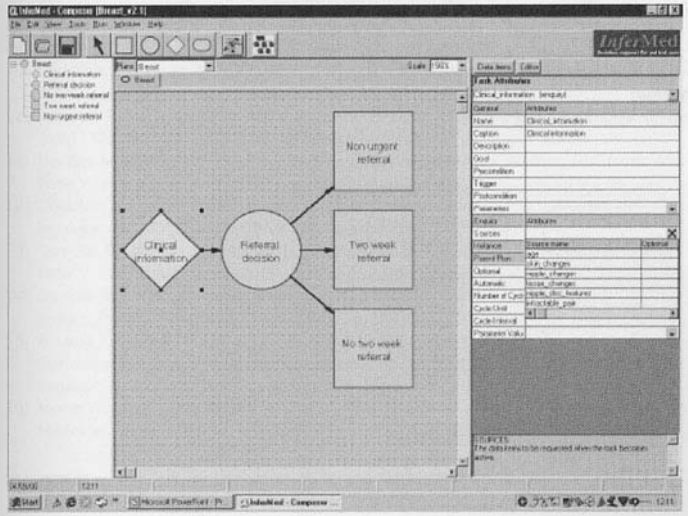
guildline
GLIF

Pro*forma* and
Solo

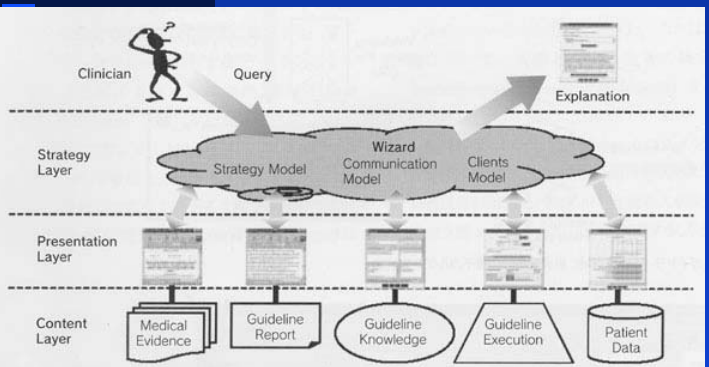




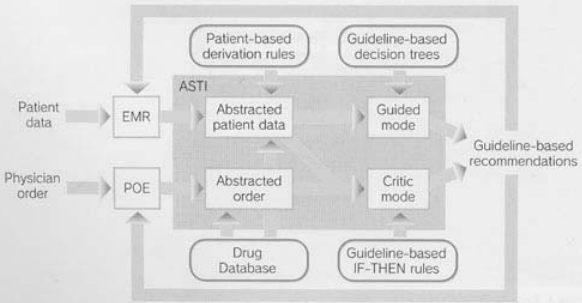
❸ 自然語のガイドラインからXML形式変換後の電子カルテとの統合



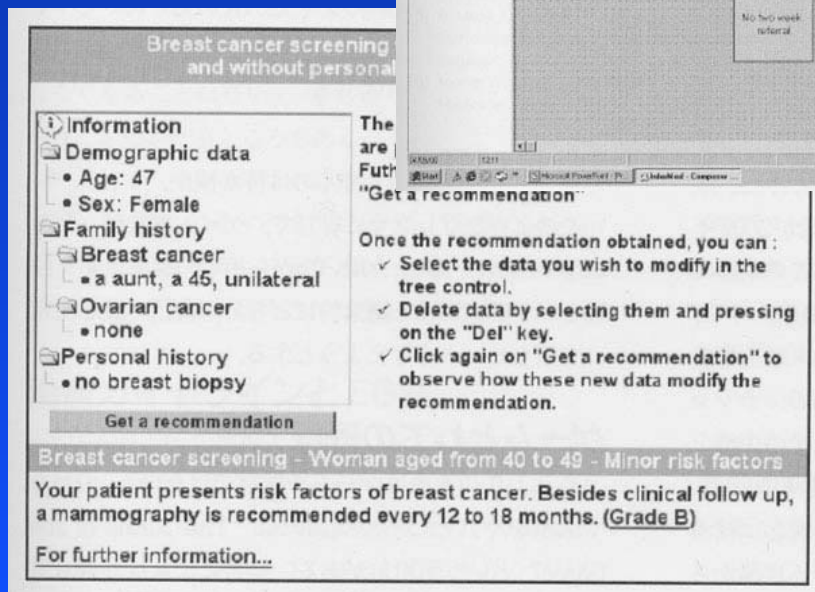
EsPeR project
Breast cancer suppo



❺ ATHENA DSSでの診療支援層構成
患者データとガイドライン知識の統合が結論の説明を生成する.



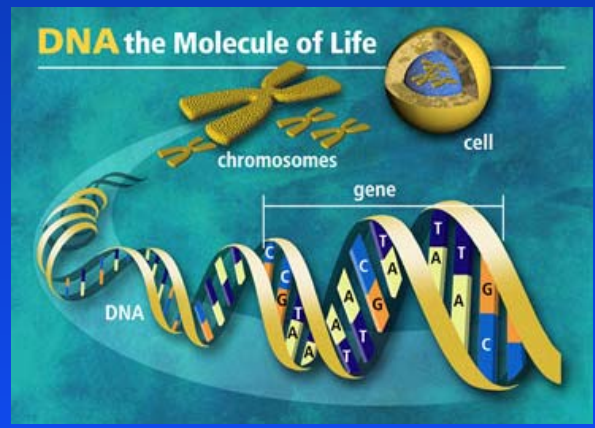
❻ ガイドライン準拠の投薬支援システムASTI



Medical IT for Genome-based Medicine

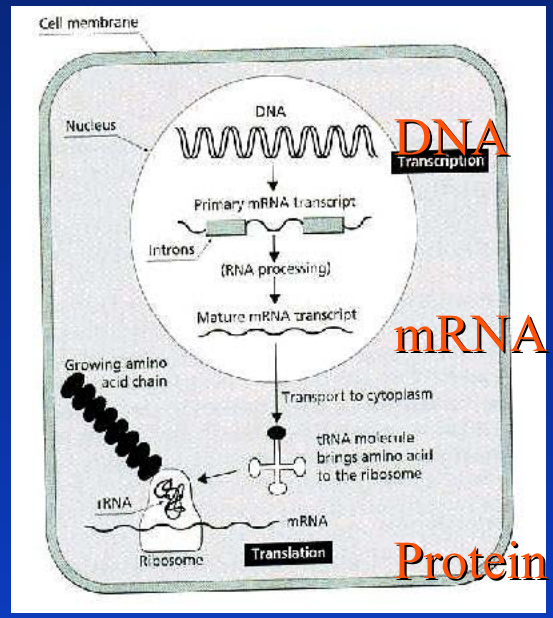
Genome sciences open New disciple

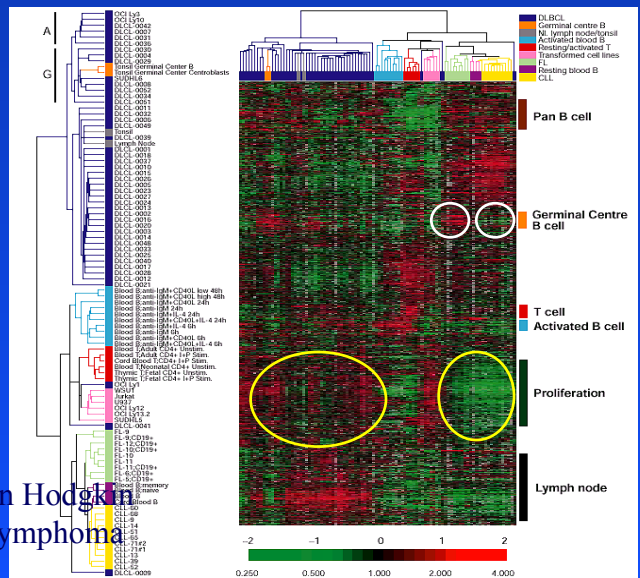
- Human Genome project is completed at 2003.4
  - 1988/90 start (HUGO)
  - 2001 3Gbp Draft Sequence
- HG opens the new field for clinical medicine
- Specially 3 fields make influences to medicine



Successive projects to '-Omics'

- Next to genome
- Transriptomics
  - mRNA (cDNA library)
  - Microarray for gene expression
    - Comparative expression
  - Diagnosis: Cancer subtype diagnosis
- Proteomics
  - Maldi/seldi TOF-MS
  - Peaks and amplitude
  - Diagnosis: cancer subtype diagnosis
- Metabolomics
  - whole metabolic molecules
  - Pattern analysis, PCA

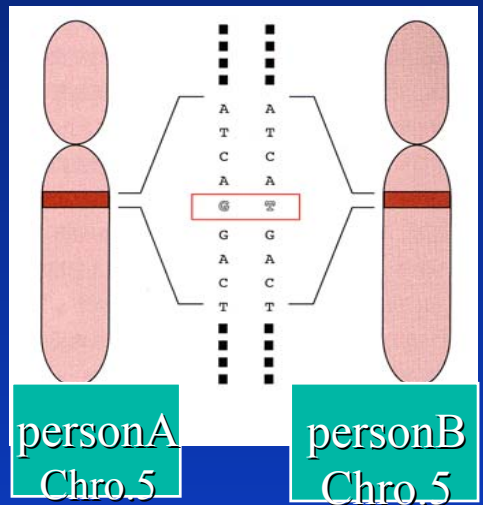


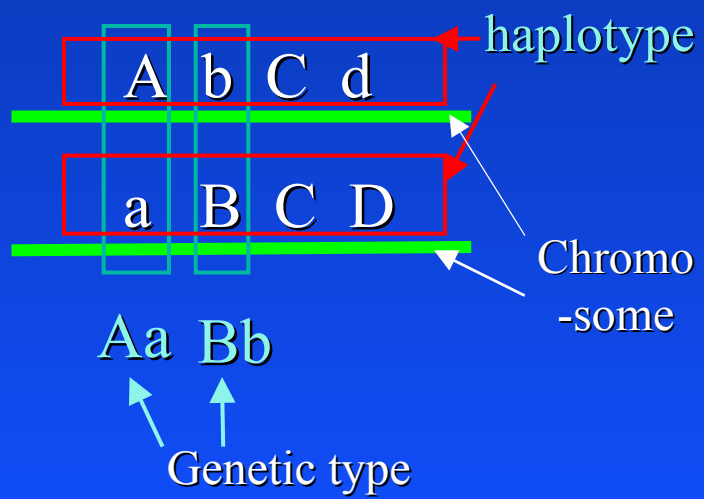


Non Hodgkin Lymphoma

Polymorphism and genomic typing

- Genomic polymorphism
  - SNP
    - single nucleotide polymorphism
    - 1 for 1000bp (0.1%) cSNP, gSNP
  - Micro-satellites, VNTR
- Linkage with
  - Disease susceptibility
  - Drug response
- Genomic Preventive medicine
  - Risk appraisal for disease incidence
- Phamacogenetic/genomic prediction
  - Prediction of drug response
- Personalized genomic typing
  - Haplotype estimation





Understanding life/disease as a system

- Pathway/network analysis
  - Genetic network
  - Metabolic pathway
  - Signaling pathway
- Systems biology
  - To understand life (cellular process) as a system
- Disease modeling/simulation
  - "Common disease"
    - System failure of signaling pathway
    - Diabetes type II; signaling failure of β cell
    - Syndrome X (High BP, Atherosclerosis, Diabetes..)

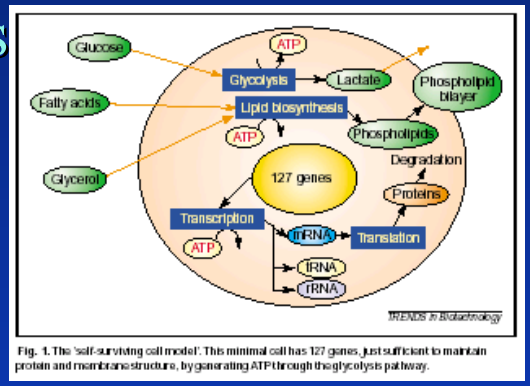
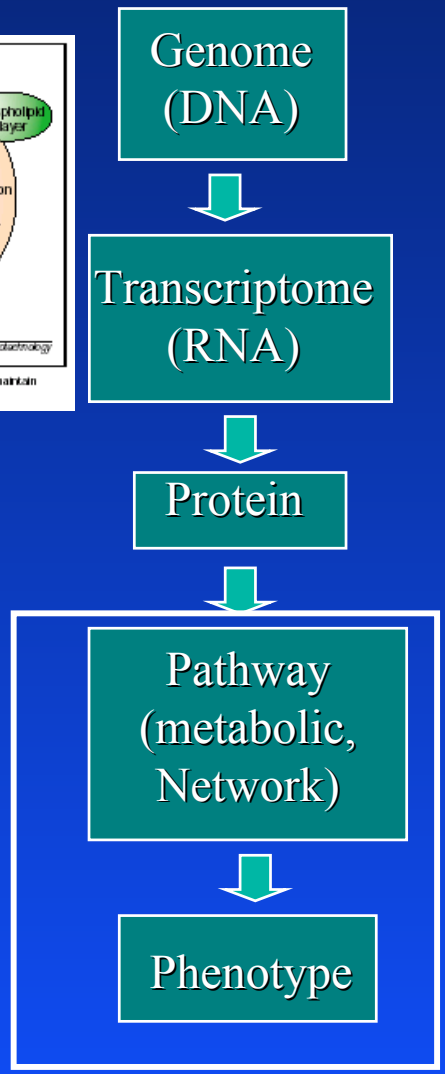
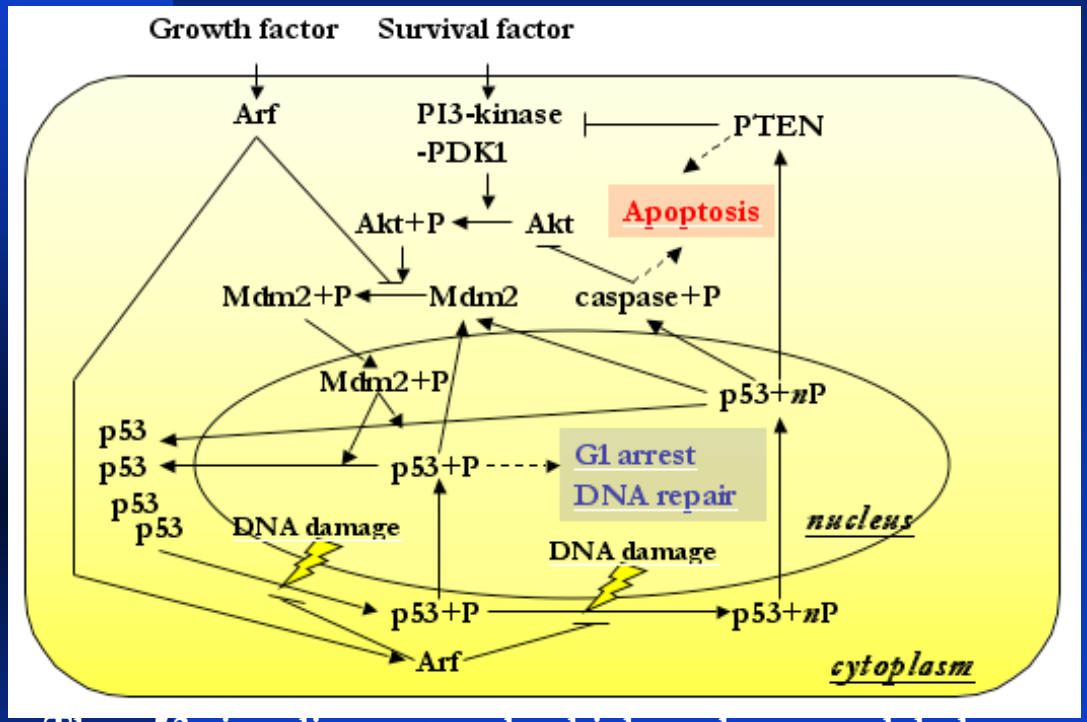


Fig. 1. The 'self-surviving cell model'. This minimal cell has 127 genes, just sufficient to maintain protein and membrane structure, by generating ATP through the glycolysis pathway.



Modeling of the p53 signaling network

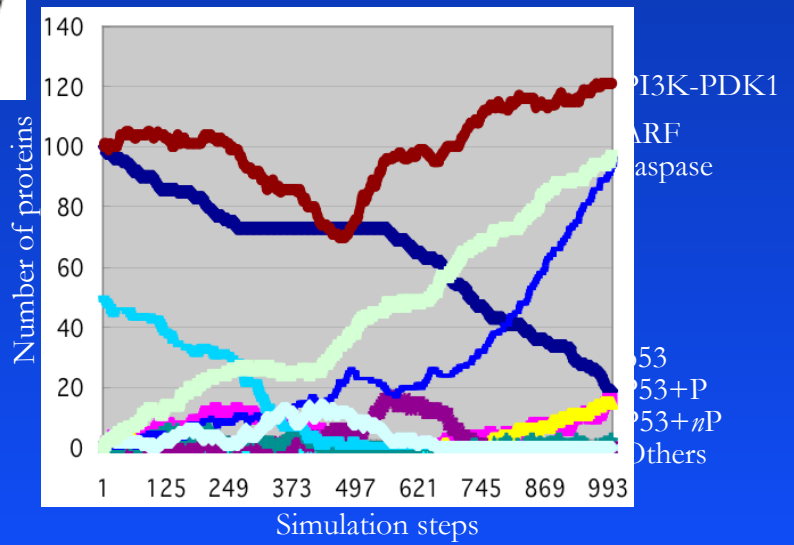


The p53 signaling network which we have modeled

to reveal its complex behaviors

- in both a **limited amount of molecules** and a **limited size of space**
- in a **discrete quantity**
- with considering **sub cellular localization** and **translocation** of molecules.

Results of this simulation



Reaction rules (partial)

nucleus

- DNA damage → DNA damage, p53 activation signal

cytoplasm

- p53 activation signal, p53×4 → p53+P

implemented by Abstract Cell Model (Suzuki Y, Ogishima S, Tanaka H)

Genome-based Medicine need IT for its realization

- Preventive
  - Risk appraisal for future disease incident together with environmental factors
- Diagnostics
  - Classification forDisease/Nondisease, Disease subtype
  - Rule extraction for diagnosis
- Therapeutics
  - Drug responder/nonresponder prediction
- For all above
  - disease pathway analysis
  - In silico simulation

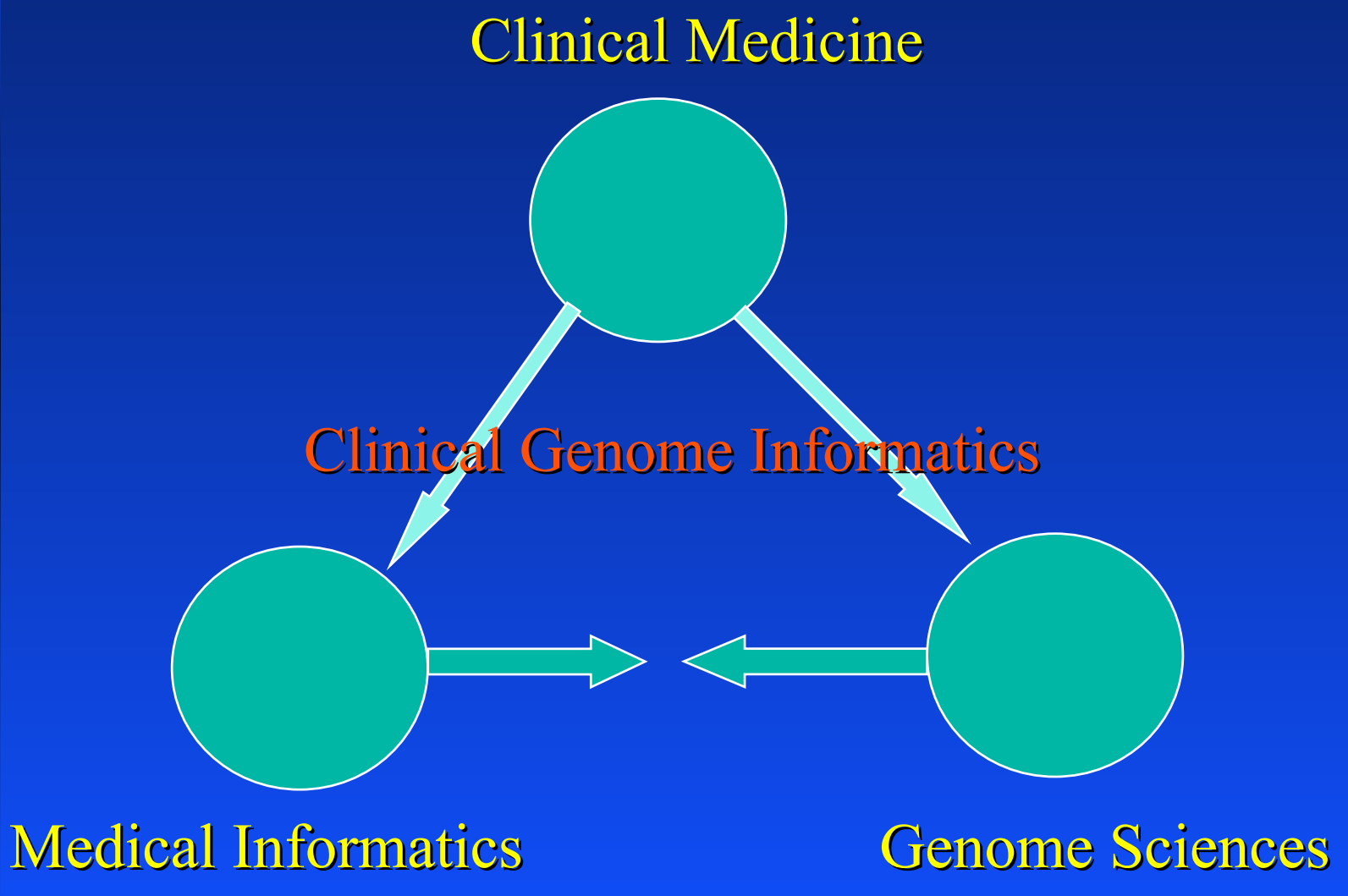
IT system

Genomic Prognostics
Genomic EMR
DSS for GBM
GB Systems analysis
Disease simulation

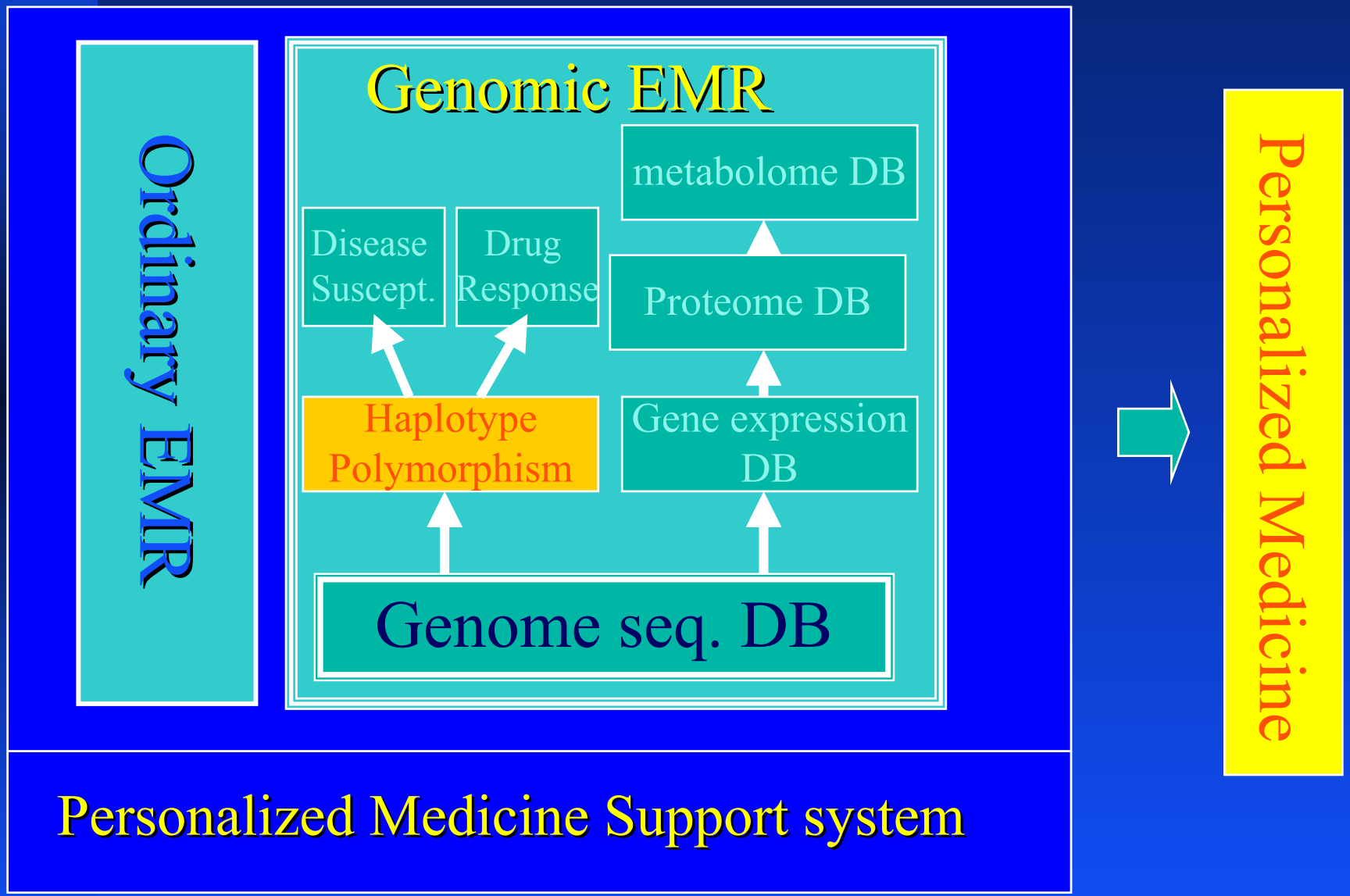
Genome-based medicine soon coming

- Immediately
  - Genomic typing for drug responder/ nonresponder becomes compulsory (FDA guidance ~ 2004)
- Coming soon
  - Proteome Cancer diagnosis (Seldi TOF-MS)
  - Microarray Cancer diagnosis
- Near future
  - Risk appraisal for incident of "common disease" based on haplotyping
  - In silico disease simulation

Future in Genome-based Medicine



Future Image of Genome-based Medicine

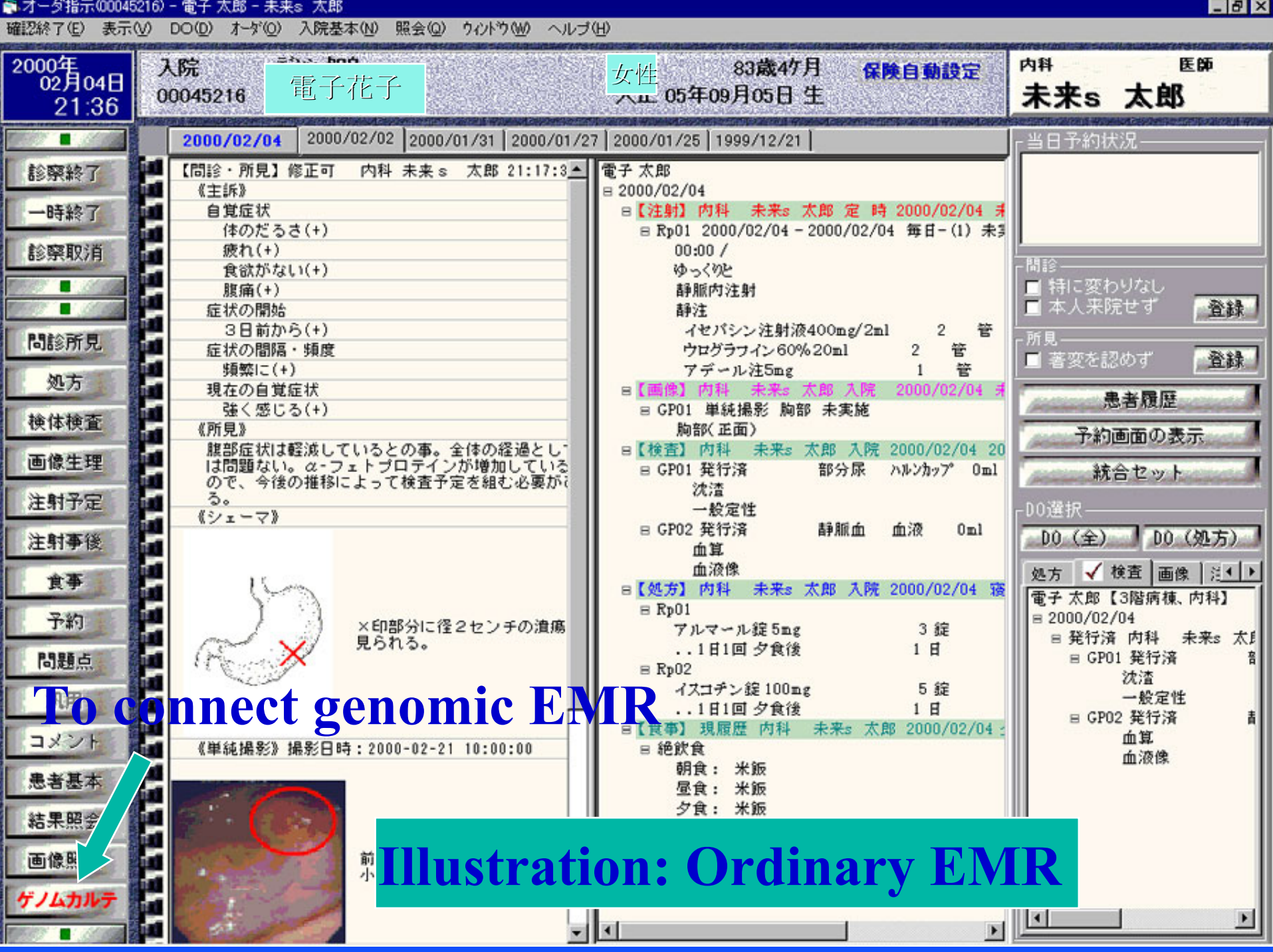


Genomic EMR system

- Genomic EMR
  - Genome Electronic Record
    - Core: Whole genome sequence
    - Multileveled Omic DB
      - Proteome, Metabolome, Array data
    - Polymorphism DB
      - haplotype,
      - drug/disease-related SNPs
  - Clinical Electronic Record
    - Ordinary EMR, patient disease history
- Personalized Medicine Support system
  - genomic diagnosis/therapy support

Genome viewer

- Whole genome view
  (Chromosomal view)
- Organ-oriented view
  (Body map view)
- Disease-oriented view
  (Disease-related view)


オーダ指示(00045216) - 電子 太郎 - 未来s 太郎
確認終了(E) 表示(V) DO(D) オーダ(O) 入院基本(N) 照会(Q) ウィンドウ(W) ヘルプ(H)
2000年 02月04日 21:36
入院
00045216
電子花子
女性
83歳4ヶ月
保険自動設定
05年09月05日 生
内科
医師
未来s 太郎
2000/02/04
2000/02/02
2000/01/31
2000/01/27
2000/01/25
1999/12/21
診察終了
一時終了
診察取消
問診所見
処方
検体検査
画像生理
注射予定
注射事後
食事
予約
問題点
コメント
患者基本
結果照会
画像照
ゲノムカルテ
【問診・所見】修正可 内科 未来ｓ 太郎 21:17:3
《主訴》
自覚症状
体のだるさ(+)
疲れ(+)
食欲がない(+)
腹痛(+)
症状の開始
３日前から(+)
症状の間隔・頻度
頻繁に(+)
現在の自覚症状
強く感じる(+)
《所見》
腹部症状は軽減しているとの事。全体の経過とし
は問題ない。α-フェトプロテインが増加してい
ので、今後の推移によって検査予定を組む必要が
る。
《シェーマ》
×印部分に径２センチの潰瘍
見られる。
《単純撮影》撮影日時：2000-02-21 10:00:00
前
小
電子 太郎
2000/02/04
【注射】 内科 未来s 太郎 定 時 2000/02/04
Rp01 2000/02/04 - 2000/02/04 毎日 - (1) 未
00:00 /
ゆっくりと
静脈内注射
静注
イセパシン注射液400mg/2ml 2 管
ウログラフイン60%20ml 2 管
アデール注5mg 1 管
【画像】 内科 未来s 太郎 入院 2000/02/04
GP01 単純撮影 胸部 未実施
胸部(正面)
【検査】 内科 未来s 太郎 入院 2000/02/04 20
GP01 発行済 部分尿 ハルンカップ 0ml
沈渣
一般定性
GP02 発行済 静脈血 血液 0ml
血算
血液像
【処方】 内科 未来s 太郎 入院 2000/02/04 寝
Rp01
アルマール錠 5mg 3 錠
..1日1回 夕食後 1 日
Rp02
イスコチン錠 100mg 5 錠
..1日1回 夕食後 1 日
【食事】 現履歴 内科 未来s 太郎 2000/02/04
絶飲食
朝食： 米飯
昼食： 米飯
夕食： 米飯
当日予約状況
問診
特に変わりなし
本人来院せず
登録
所見
著変を認めず
登録
患者履歴
予約画面の表示
統合セット
DO選択
DO（全）
DO（処方）
処方
検査
画像
電子 太郎【3階病棟、内科】
2000/02/04
発行済 内科 未来s 太
GP01 発行済
沈渣
一般定性
GP02 発行済
血算
血液像
To connect genomic EMR
Illustration: Ordinary EMR

オーダ指示(00045216) - 電子 太郎 - 未来s 太郎

確認終了(E) 表示(V) DO(D) オーダ(O) 入院基本(N) 照会(Q) ウィンドウ(W) ヘルプ(H)

2000年 02月04日 21:36

入院 00045216 電子花子 女性 83歳4ヶ月 大正 05年09月05日 生 保険自動設定

内科 医師 未来s 太郎

Chromosomal view

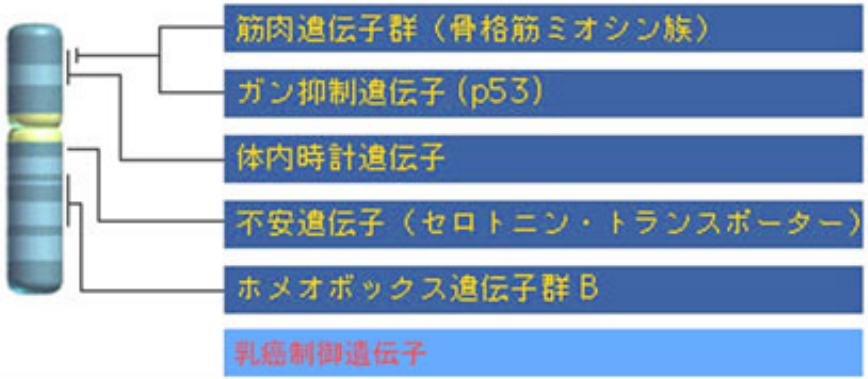
ゲノム総覧 | 臓器別 | 疾患別

診察終了 / 一時終了 / 診察取消 / 問診所見 / 処方 / 検体検査 / 画像生理 / 注射予定 / 注射事後 / 食事 / 予約 / 問題点 / 汎用 / コメント / 患者基本 / 結果照会 / 画像照会 / ゲノムカルテ

ゲノムカルテ

ゲノム総覧 VIEW

第17染色体



乳癌制御遺伝子

BRCA1 欠損マーカー ＋ **要精密検査**

参考

BRCA1の欠損を示すマーカーをもつ女性の場合、乳癌の発症率は50歳で59%(平均は2%)65歳で80(平均は%5%)に達する。

問診: 特に変わりなし / 本人来院せず 登録

所見: 著変を認めず 登録

患者履歴 / 予約画面の表示 / 統合セット

DO選択: DO（全） DO（処方）

処方 | 検査 | 画像

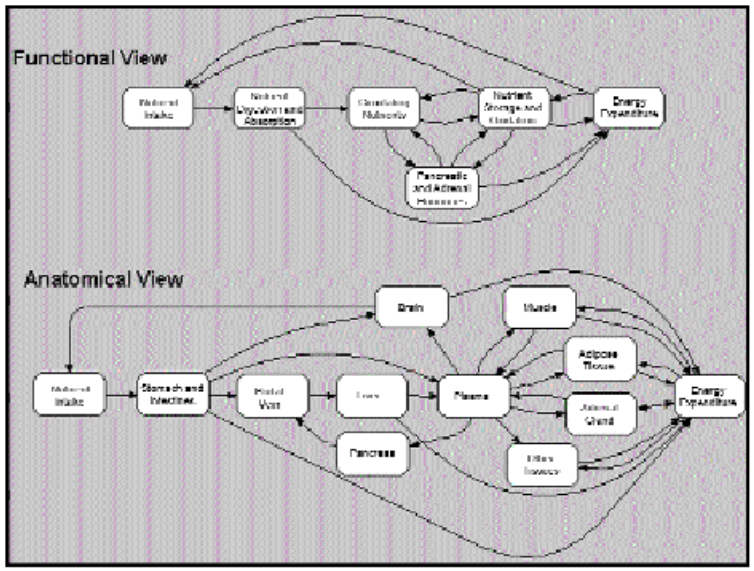
電子 太郎【3階病棟、内科】
2000/02/04
発行済 内科 未来s 太郎
GP01 発行済
沈渣
一般定性
GP02 発行済
血算
血液像

In silico disease simulation

Building the Diabetes PhysioLab™

They applied a top-down approach, focusing first on the clinical outcomes, next on defining the largest physioloigcal systems and functions involved in the disease, and then adding detail and breadth. This is an iterative process that involves:

1. identifying characteristic behaviors of the disease
2. creating a mathematical model of the physiologic systems necessary to represent those behaviors
3. validating the model based on published

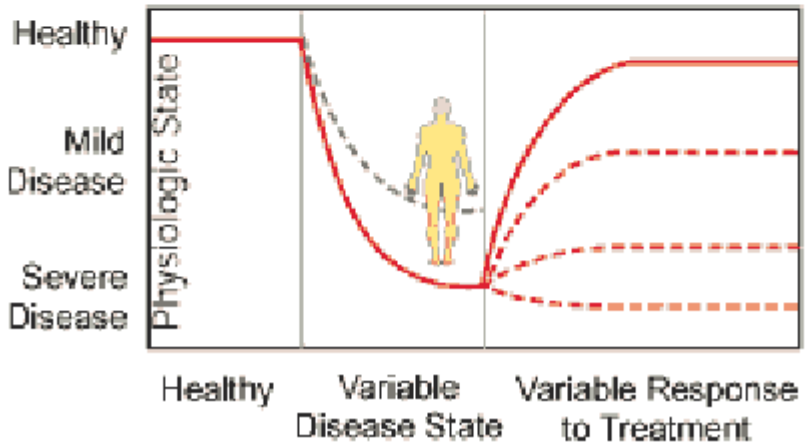


Summary Diagram of Entelos® Diabetes™ PhysioLab Disease Map. Each node (bubble) points to more detailed diagrams in the model. There are approximately 75 diagrams within the complete disease map.

Creating Virtual Patients

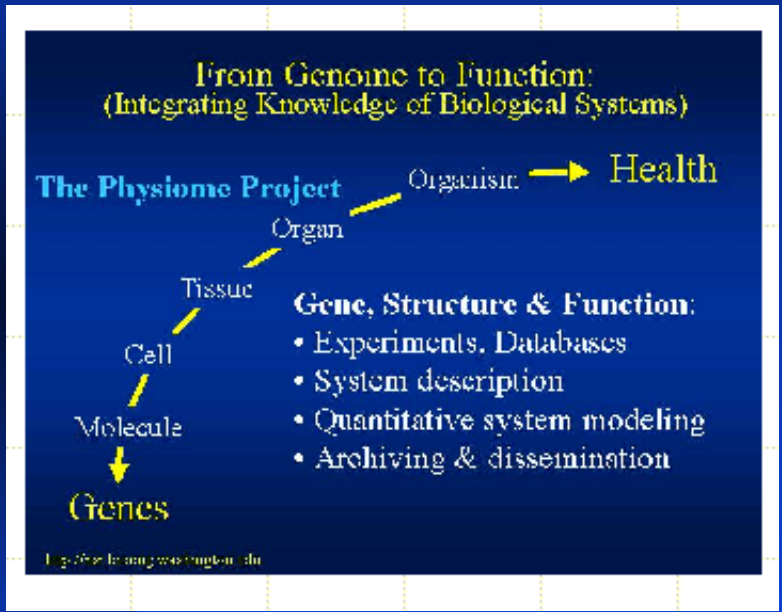
Each PhysioLab™ model is first built to represent normal, healthy physiology. Virtual patients are then created within the model to represent the many and varied forms of the disease state.

Virtual Patients:
Development and Response

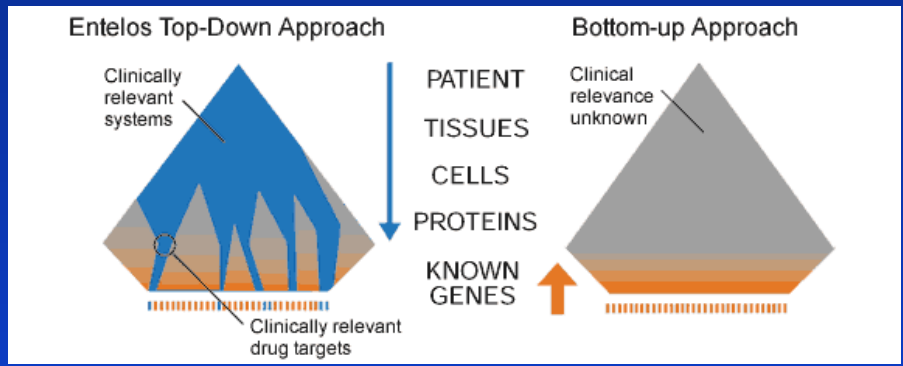


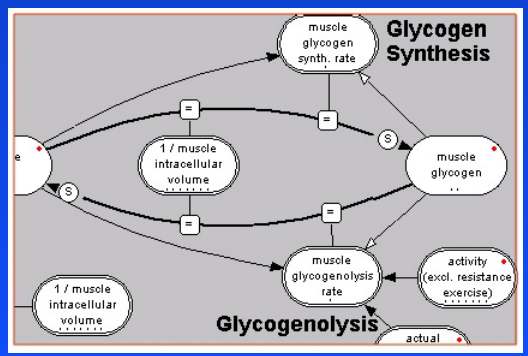
Hierarchial Medel

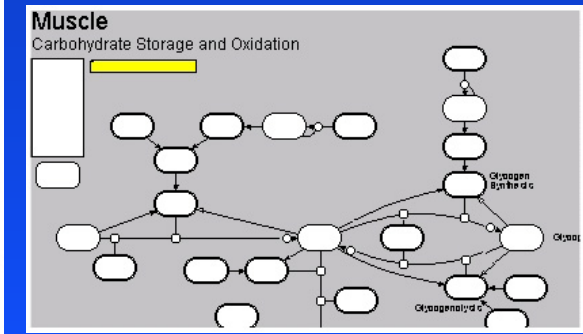
Physiome project



Entelos





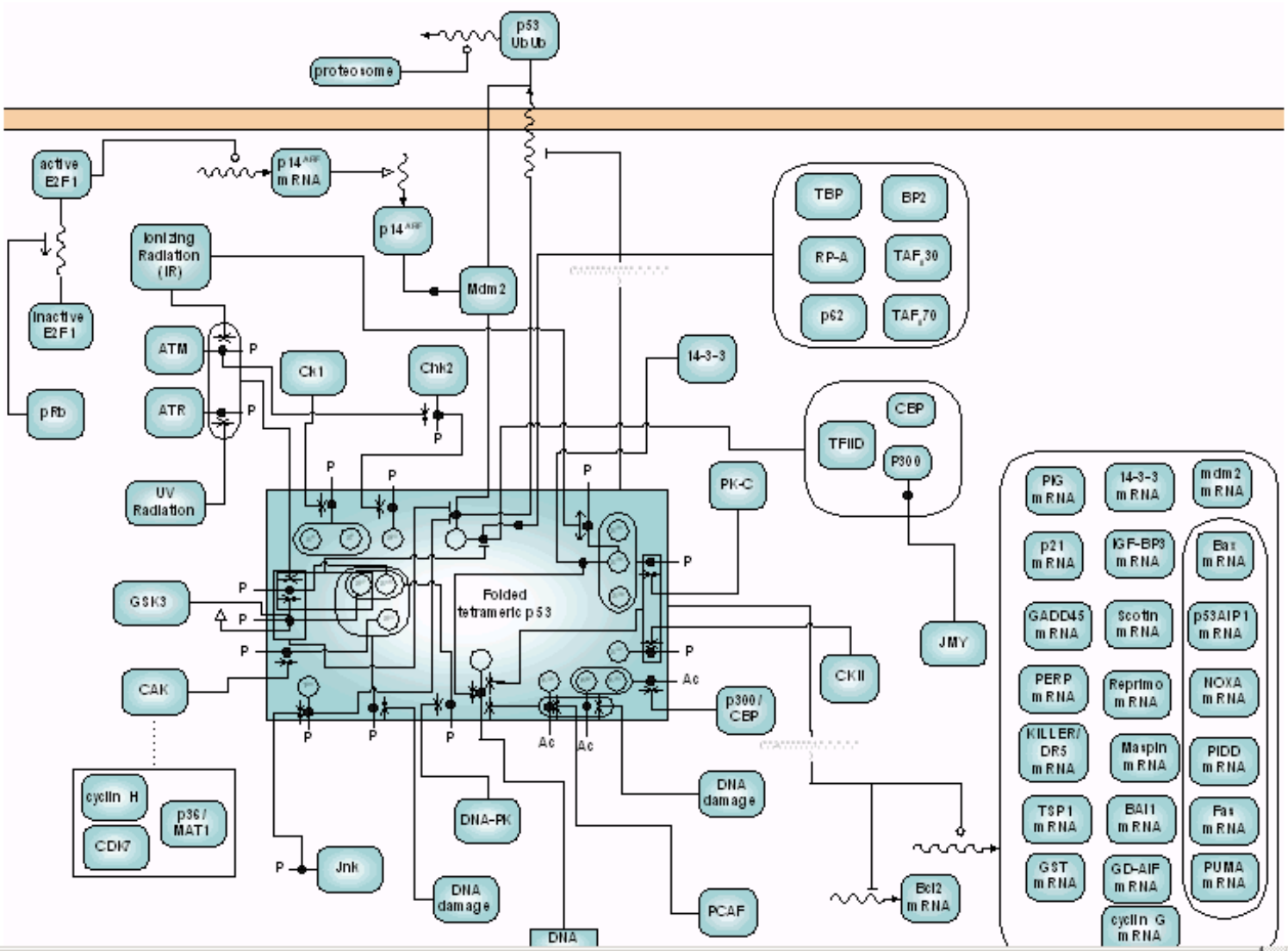


Gene Network Sciences, Simulating Life for Drug Discovery - Microsoft Internet Explorer

ファイル(F) 編集(E) 表示(V) お気に入り(A) ツール(T) ヘルプ(H)

アドレス(D) http://www.gnsbiotech.com/applications.shtml 移動 リンク 戻る

p53, The gatekeeper of death:



インターネット

Conclusion

- Standardized and Personalized Medicine are the Key concept for 21th medicine
- Both need Medical IT to realize itself.
- Computerized EBM and Genome-based Medicine is new challenges for Medical IT,

  though still firm design concept is lacking now
- Situations are changing rapidly than we expect, so that we should tackle them immediately