LABORATORY MEDICINE: PAST, PRESENT AND FUTURE

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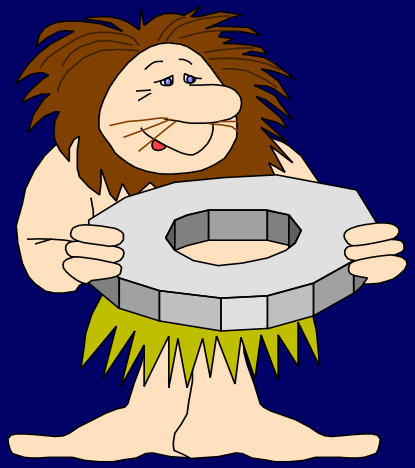
DISCUSSION

A few reflections on the

Past and Present

Future



DISTANT PAST!
First tests known

Diabetes

Patient urinates on the floor. If the urine contains sugar, ants will crawl to lick the urine. This test was used up to 20 years ago in some parts of Africa

PHLEBOTOMY

- In the 20th century phlebotomy was introduced as a diagnostic tool
- Prior to that it was considered to be curative

EXAMPLES OF PHLEBOTOMY FOR CURING PATIENTS

- 16th century Italy, physicians would order 15-20 leeches per hospital patient before examining them
- George Washington, the first US President, probably had only a common cold when he was bled daily as a treatment. It is thought that he died due to excessive blood loss

INSTRUMENTATION IN LABORATORY MEDICINE: 1920

A modern 200-300 bed hospital in the USA would be well equipped if it had. .

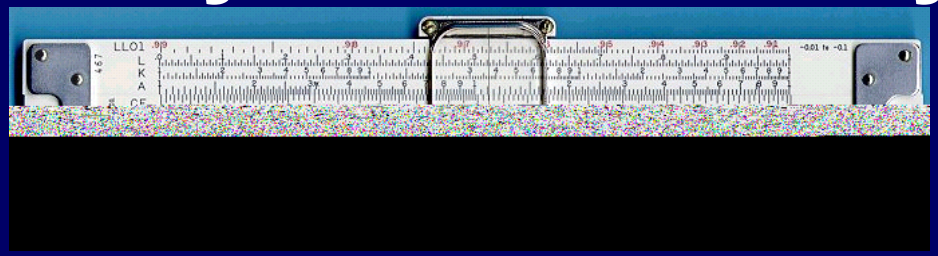
- A balance
- A microscope
- A centrifuge
- A Bunsen burner
- A Duboscq colorimeter

CLINICAL CHEMISTRY IN A HOSPITAL LABORATORY 1970

- Balance
- Spectrophotometer
- Flame photometer
- Van Slyke apparatus
- Klett colorimeter
- Centrifuge

IN 1970

- There were no calculators. Slide rules were used!
- No automation
- No sophisticated quality control
- No fax machines
- No laboratory information systems



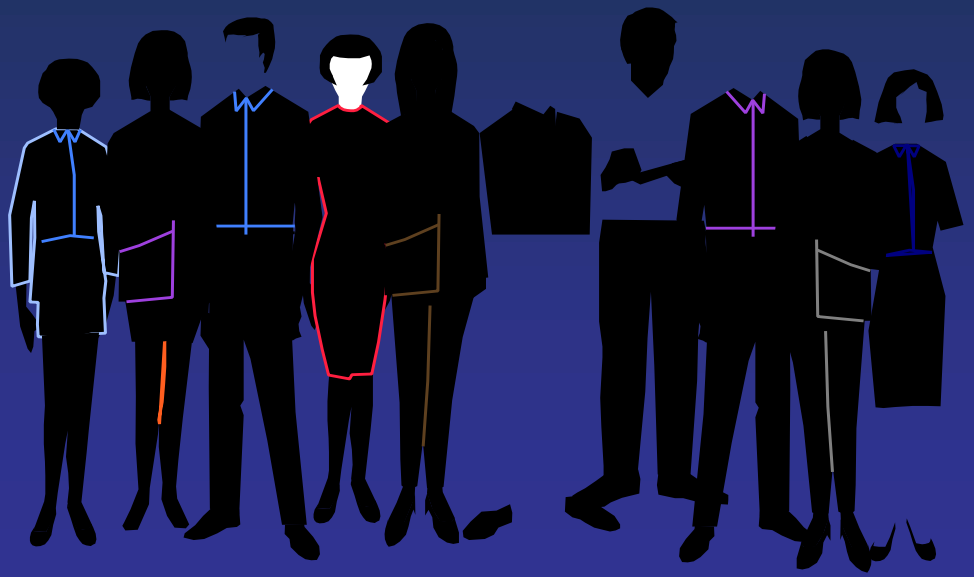
PRESENT

- Point-of-Care Testing
- Molecular diagnostics
- Sophisticated equipment such as Tandem Mass Spectrometry
- Consolidation of testing on a single platform
- Consolidation of reference laboratories

THE NEAR FUTURE

- Short staffing
- Dramatic increase in POCT and home testing
- Non invasive testing
- Increased use of Tandem Mass Spectrometry
- Use of Molecular Diagnostics (Chips and SNPs), single cell analyses
- Use of robotics
- Working from home: telecommuting

STAFFING PROBLEMS

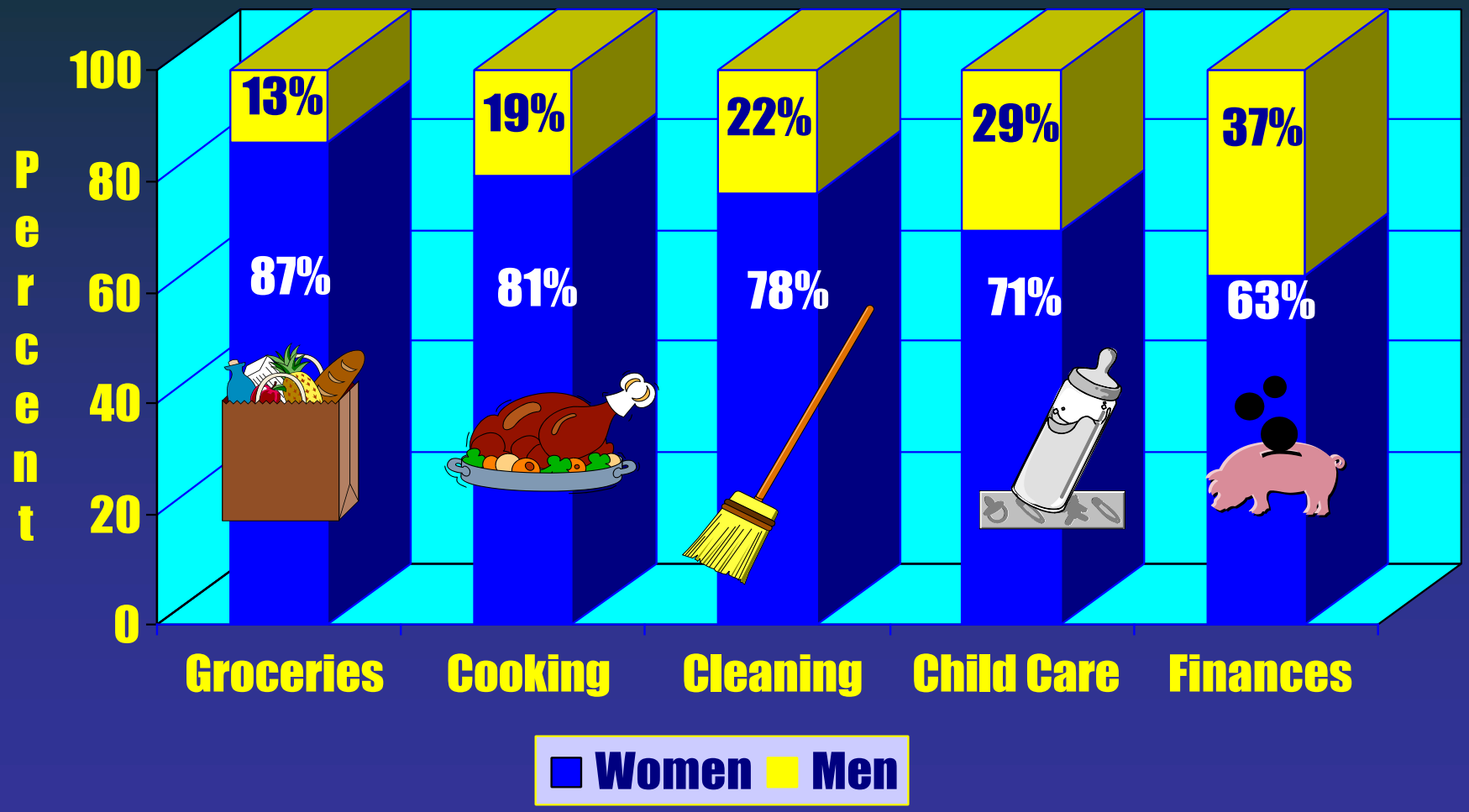


STAFFING PROBLEMS

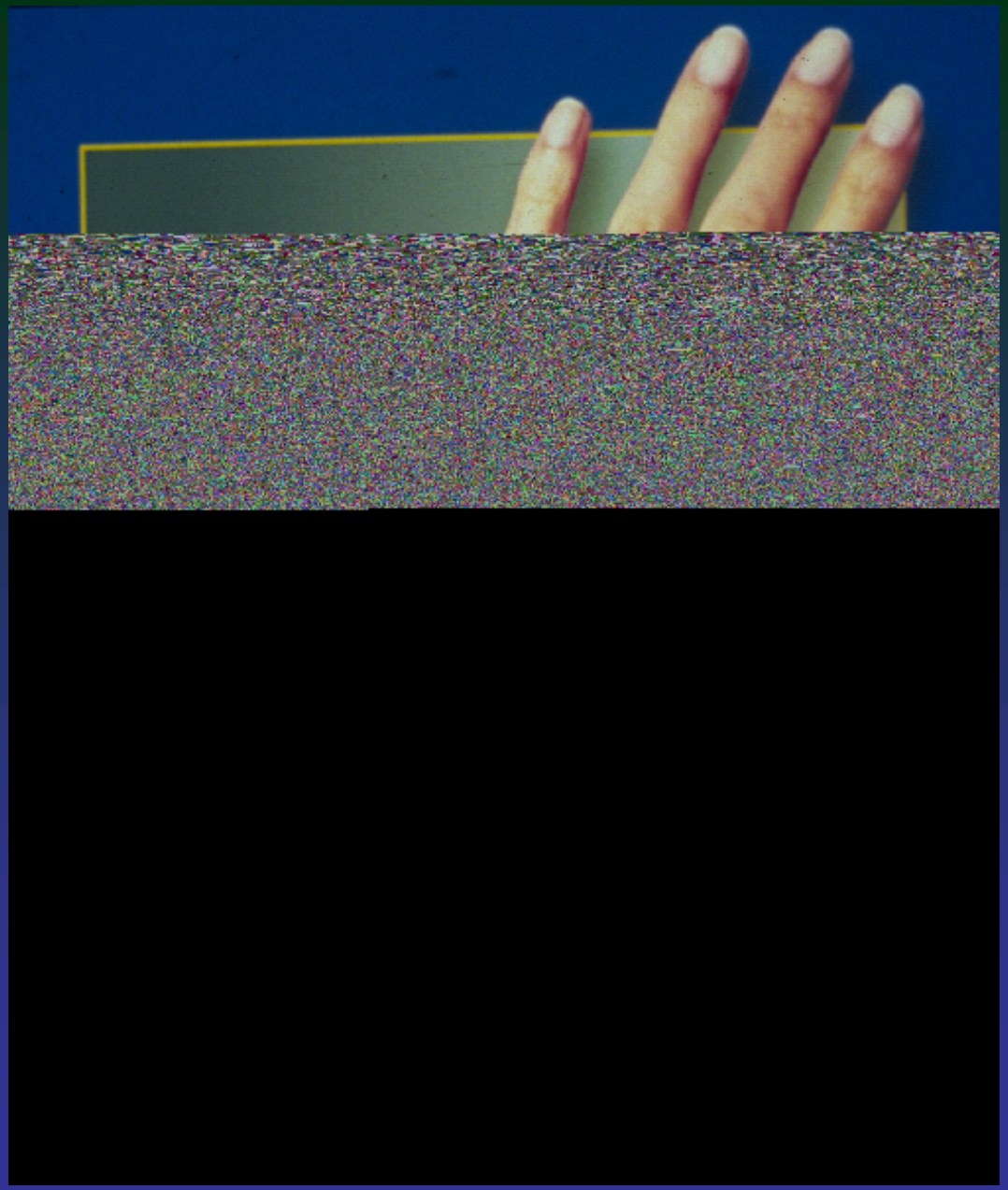
Staffing shortage of 13% nationwide in the USA! *WHY*?

- ➔ **Medical technology schools closing**
- ➔ **Laboratory Medicine technologists and technicians mostly women**
- ➔ **Women going into different fields**
- ➔ **Aging staff..average age nationwide is 51y old**

DUAL INCOME FAMILIES (USA)
Home responsibilities

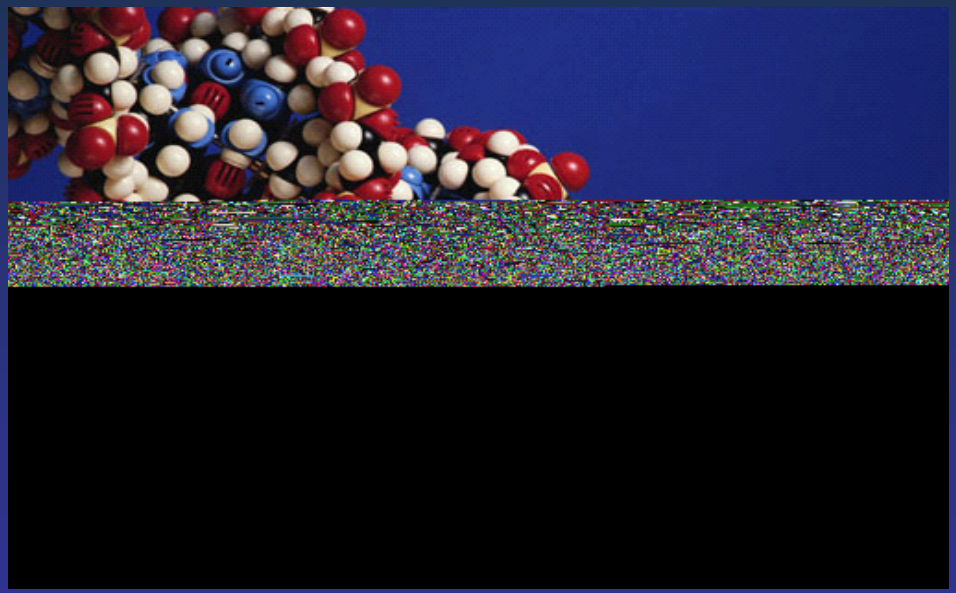


NON INVASIVE TESTING



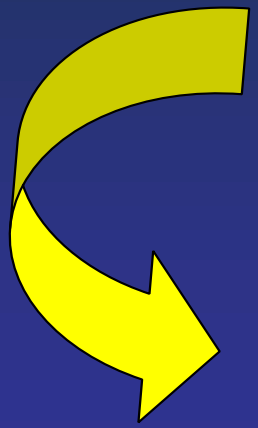
GLUCOWATCH

MOLECULAR DIAGNOSTICS

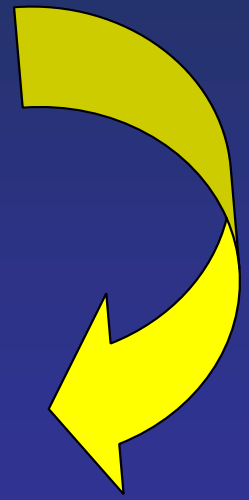


THE IMPORTANCE OF MOLECULAR DIAGNOSTICS

Lab results determine how 70% of healthcare dollars are spent	Molecular diagnostics is the fastest growing field within laboratory testing



Molecular diagnostics gives clinical practitioners more knowledge, better odds to fight and prevent disease



MOLECULAR DIAGNOSTICS: BETTER PATIENT CARE

- Infectious Disease & Resistance Testing
- Disease Prevention
- Personalized Medicine
- Technology Requirements:
  1. Certainty
  2. Control
  3. Consolidation

MOLECULAR DIAGNOSTICS

Single Cell Analyses

PREIMPLANTATION GENETIC DIAGNOSIS (PGD)

Offers an alternative to traditional methods of prenatal diagnosis including chorionic villus sampling and amniocentesis

PREIMPLANTATION GENETIC DIAGNOSIS (PGD)

Allows genetic analysis and selection of embryos to be performed

prior to implantation and pregnancy, and thereby increasing the possibility of a child free of Genetic Disease

REQUIRES THE FOLLOWING STEPS…

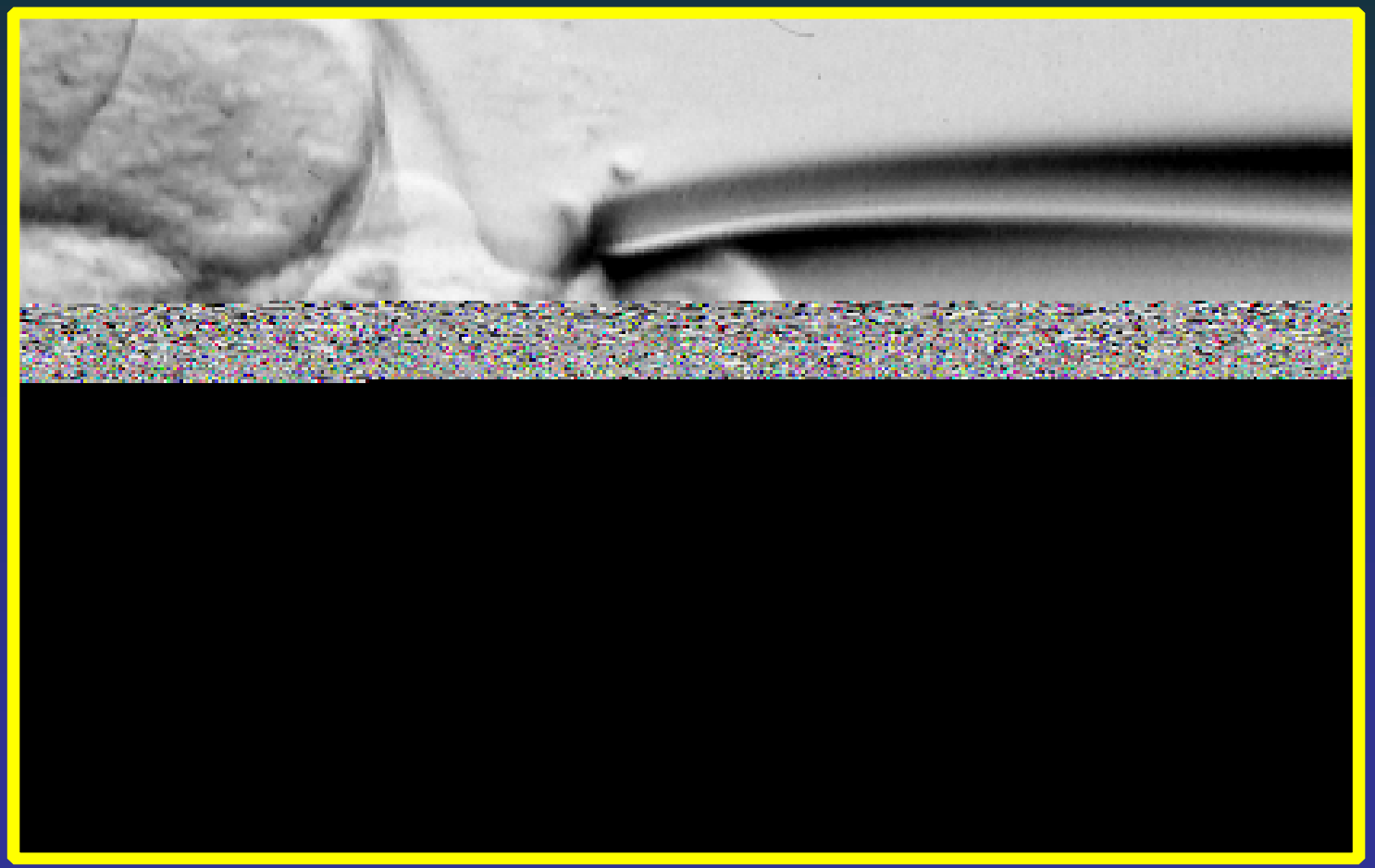
- Production of embryos following a routine IVF cycle
- Growth of the embryos to ~8 cells (day 3)
- Biopsy (removal) of embryonic cells (blastomeres) for testing
- Capture of DNA (for PCR based tests) or intact nucleus (for FISH based tests)

PGD:REQUIRES THE FOLLOWING STEPS...

- Amplification of DNA (PCR based tests) or hybridization of fluorescently labeled DNA probes (FISH based tests)
- Interpretation and reporting of results
- Transfer of selected embryos into uterus on day 5 post retrieval

EMBRYO BIOPSY

EMBRYO BIOPSY



PGD: NEW YORK TIMES SEPT 3, 2006

Article about a couple culling embryos obtained by in vitro fertilization to halt the strong heritage of Colon Cancer

- **Is this unnatural selection or a wise decision in being sure their offspring does not carry the colon cancer gene?**
- **Is it a "pact with the devil" and "discriminatory" and producing designer babies, or is it right for persons to try to avoid deadly diseases in their progeny?**

MOLECULAR DIAGNOSTICS

The Use Of DNA Chips

BENEFITS OF CHIP PLATFORMS

- Combine all testing needs on one platform
- Cost-per-test decreases
- Test flexibility means lab can meet increasing test demands
- Technologist time is reduced
- One workstation means less bench space is occupied

THE "-OMICS" REVOLUTION

- ✓ Proteomics
- ✓ Pharmacogenomics
- ✓ Physiogenomics
- ✓ Nutrigenomics

PROTEOMICS

- It is the large scale study of proteins, particularly their structure and functions
- The proteome is complex. It varies from cell to cell, and is constantly changing through its biochemical interactions with the genome and the environment
- The study of proteomics can lead to a better understanding of the disease process
- To catalog all human proteins is a major challenge for scientists. There is an international collaboration to achieve this goal that is being coordinated by the Human Proteome Organization

KEY TECHNOLOGIES used in PROTEOMICS

- One and two dimensional electrophoresis
- X-ray crystallography and magnetic resonance
- Tandem mass spectrometry
- Mass spectrometry
- Affinity chromatography
- X-ray tomography
- Software based image analysis

PHARMACOGENOMICS: THE LATEST!

- Pharmacogenetic tests can predict whether a drug will be effective or cause adverse, or even deadly side effects
- This especially applies to psychiatric and cardiac drugs
- Approximately 70 drugs have been identified that are catabolized by cytochrome P450 enzymes. There is now a test for these enzymes. More than 50 variations are known of the 2D6 gene that controls these enzymes

PHYSIOGENOMICS: RECENT REPORTS

Serum albumin-bound fragments: An archive of Potential Disease Markers

1. A protein fragment has been identified, which is derived from a protein encoded by the BRCA2 cancer associated gene
2. Protein markers have been identified for Alzheimer's Disease

1) Lowenthal MS, et al. Clin Chem 2005; 51:1933-45
2) Lopez MF, et al. Clin Chem 2005; 10:1946-54

NUTRIGENOMICS

- It is the field that examines the response of individuals to compounds in food using genomic and other related technologies

- "Nutrigenomics research looks at how diet interacts with gene expression"

NUTRIGENOMICS Cont'd

- ✓ Identifying poor folate metabolizers
- ✓ Testing involves folate metabolism and the gene for 5,10-methylenehydrofolate reductase (MTHFR). This enzyme converts 5,10-methylenetetrahydrofolate to 5-methyltetrahydrofolate
- ✓ Mutations of the MTHFR gene are associated with homocystinemia, a risk factor for spina bifida births in pregnant women and premature cardiac disease

NUTRIGENOMICS, Cont'd

- ✓ The ultimate goal would be to have broad- based population testing for health maintenance
- ✓ However before any testing becomes widespread it will have to be more evidence based
- ✓ A concern is could information gleaned from SNPS be misused by employers?

GENOME-WIDE ASSOCIATION STUDIES

- Collecting DNA samples from populations whose clinical characteristics are well defined
- Doing cost effective genotyping and sophisticated statistical analysis
- These resources represent an essential component in establishing genes relevant to a particular disease

SUCCESSES IN GENOME-WIDE ASSOCIATION STUDIES

Identification of genes for:

- Age-related macular degeneration
- Myocardial infarction
- Abnormal cardiac repolarization intervals
- Four loci associated with type II diabetes
- The genetic risk factors identified by these studies are likely to be associated with moderate risks rather than the extremely high risks associated with single gene disorders

N. Eng. J. Med. 2007; 356: 1094-7

OTHER CHALLENGES FOR THE FUTURE

- e-Technologies
- Global harmonization of IVDs
- Use of Nanotechnology
- Efforts to reduce Laboratory errors
- A effort to decrease unnecessary tests
- The changing population demographics in the US. Ethnic, cultural and racial diversity will change the incidences of major illnesses
- International competition in healthcare

INFORMATION TECHNOLOGY(IT)

- IT needs to be the backbone of healthcare
- It can lead to a better understanding of unnecessary tests
- It allows the development of evidence-based protocols
- Leads to an understanding of the “best” laboratory tests for the diagnosis of disease

INFORMATION TECHNOLOGY

We are way behind!!

20-25% of hospitals have computerized physician order entry systems for laboratory tests, or electronic medical records

WE MUST MOVE FASTER!

THE MORE DISTANT FUTURE, BUT COMING!!

- **PERSONALIZED MEDICINE**

- **PREVENTIVE MEDICINE**

NO LONGER "ONE SIZE FITS ALL!

ADVANCING THE CONCEPT OF PERSONALIZED MEDICINE

In May 2007 The National Human Genome Research Institute (part of the National Institutes of Health) in the US announced the following initiative:

- An investigation of the interest level of healthy young adults in receiving genetic testing for eight common conditions
- This study is called the " Multiplex Initiative"

THE MULTIPLEX INITIATIVE

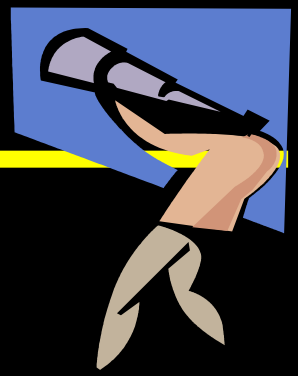
Look at the interest in information regarding 15 different genes that play roles in the following:

- Type II diabetes
- Coronary heart disease
- High blood cholesterol
- Osteoporosis
- Lung cancer
- Colorectal cancer
- Malignant melanoma

THE MULTIPLEX INITIATIVE

- This will provide insight into advancing the concept of personalized medicine
- We need to know how such susceptibility testing will be received by individuals
- We need to find out the role this type of testing will play in improving health
- Participants in the study will receive free genetic testing

PREVENTION:
BETTER MEDICINE, BETTER ECONOMIC SENSE



- **Focus on early health rather than late disease**
- **It is better medicine to prevent disease early. e.g. treat cardiac disease at the onset of symptoms of high cholesterol, high blood pressure, etc.**

FACTS re NON- PREVENTIVE MEDICINE

- Currently 70-80% of healthcare resources are spent on advanced diseases
- 70 million baby boomers (age 50y and older) are eligible for colon cancer screening. Fewer than half have complied
- The 5 year survival rate for colon cancer is 90% for localized cancer and 8% if the cancer has spread further in the body
- Breast cancer survival has improved dramatically as a result of routine mammograms

Thank you to the Turkish Biochemical Society and the Balkan Clinical Laboratories Federation for inviting me here today