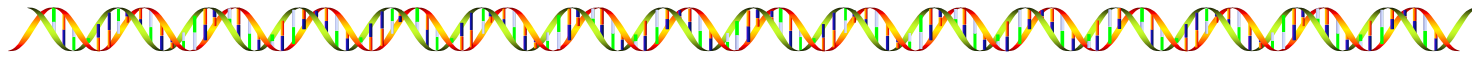


Biological Engineering Design



MIT Course 20.380

Spring Term, 2010

*John Essigmann, Darrell Irvine and Forest White
(Instructors)*

*Mya Poe, Atissa Banuazizi, and Harlan Breindel
(Writing Instructors; this is a CIM course)*

Peter DeMuth and Jesse Shapiro (Your TAs)

Today's Agenda

- Introduction of course staff
- Scientific staff expectations and grading
- CI-M staff expectations and grading
 - Course will emphasize a lot of “peer review”
- Description of R&D Consulting Concept
 - Our “organizational chart” is a matrix
 - Each student will be part of two groups
- Identify “specialty groups” that fit your goals and interests best
- Scientific staff lecture: *The immune system under normal (healthy) conditions* (Darrell)



20.380 Goal: Design of Novel Technology for Analysis of Complex Biological Systems

*Using what you learned in 20.110, 310, 320, 330,
5.07/7.05, 7.03 and 7.06*

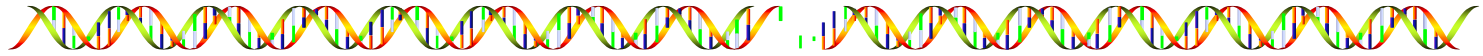


**20.380 Goal: Design of Novel
Technology for Analysis of Complex
Biological Systems**

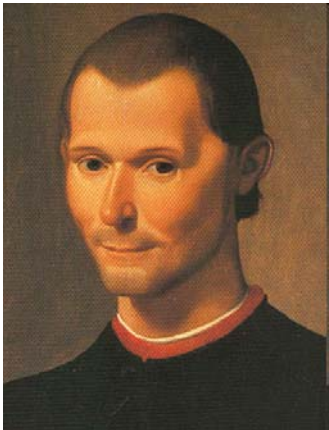
*Using what you learned in 20.110, 310, 320, 330,
5.07/7.05, 7.03 and 7.06*

Think about the meaning
of these words ...

Biological Engineering Design



*Why tackle “complex”
biological systems (usually
diseases)?*

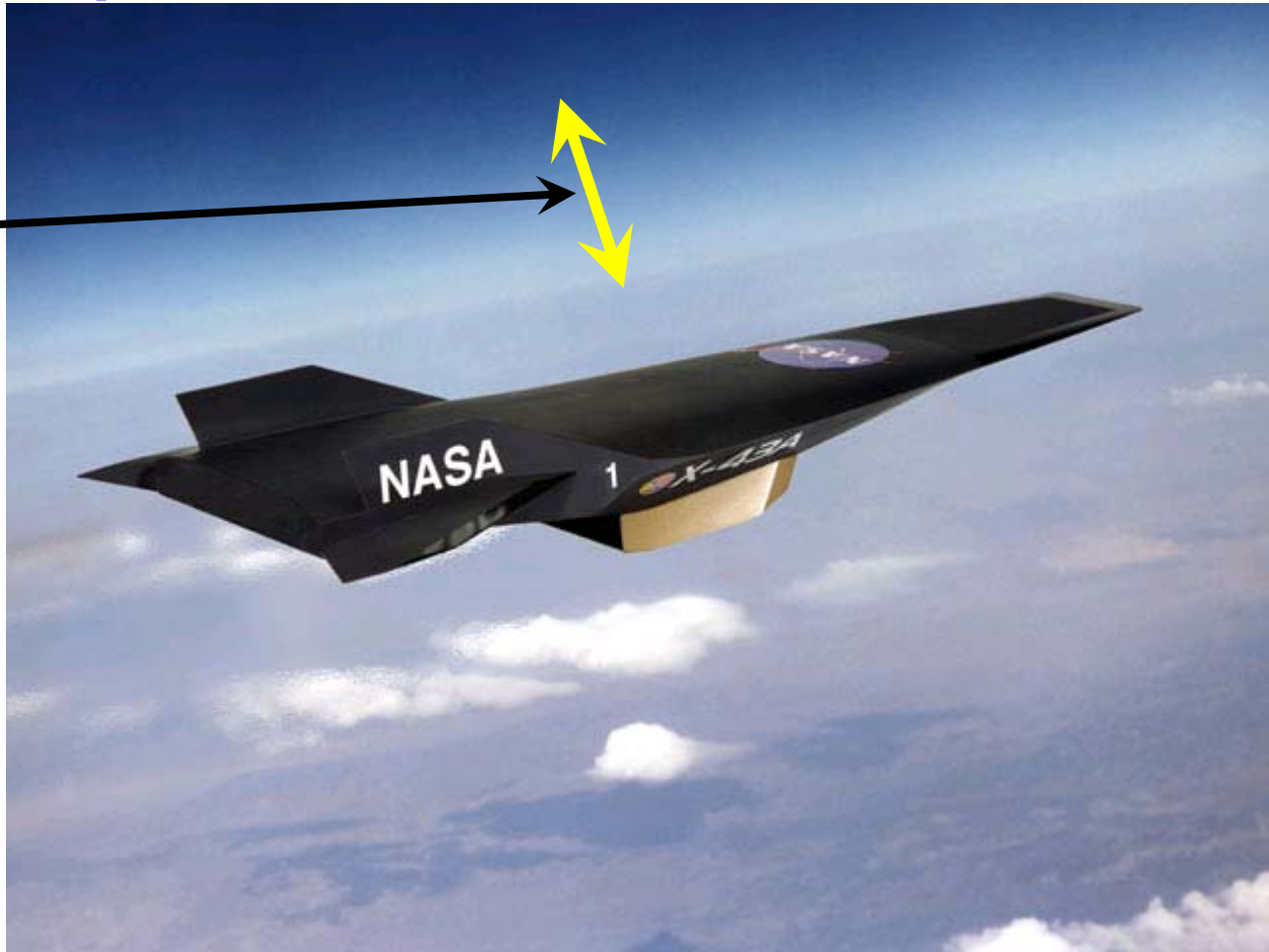


**“Make no small plans for they have
no power to stir the soul”**

Niccolo Machiavelli

Novelty: Pushing the Edge of the Envelope

Envelope



Society (Our Client) Defines Our Tasks

- This year we shall study the role of inflammation in complex diseases – such as type II diabetes, cancer and cardiovascular disease
- These diseases are bewilderingly complex
 - A lot is known but it does not all fit together (fuzzy networks)
- The easy things have been tried
 - Now we need to come up with truly novel ideas
- 20.380 teaches you how to strategize in teams to come up with novel solutions to complex problems
- The faculty have to do this every day ... this is where we teach you how to navigate the path of research design

Image removed due to copyright restrictions.

Cover of Time Magazine, February 23, 2004.
"The Secret Killer: the surprising link between inflammation and heart attacks, cancer, Alzheimer's and other diseases."

<http://www.time.com/time/covers/1101040223/>

See cover story: Gorman, C., A. Park and K. Dell.
"[Health: The Fires Within](#)." Time, February 23, 2004.

Remember the BS you put into your MIT application ... the stuff about changing the world?

- You have had all of the courses ...
- It's time for you to deliver!

20.380 Goal: Design of Novel Technology for Treatment of Incurable Diseases

Using what you learned in 20.110, 310, 320, 330, 5.07, 7.03 and 7.06

Underpinnings of 380:

hGH

- Rigorous Design – Be creative, think out of the box, develop and protect intellectual property
- Societal Need (Market) – Pick challenging opportunities for which an unmet need exists and is quantifiable; balance commercial success with altruism
- Practical Pre-clinical and Clinical Analysis – How does your device/drug/product work, how will you test it?
- Manufacturing – How will you make it? Can it be made at reasonable cost?

Design of something novel and practical ... not just reverse engineer a successful product

This is an important time of transition ...

- It is time to pull together all you know to design something practical
- This is part of your transition from MIT to what comes after MIT:
- The real world
 - Companies
 - Public service
 - Teaching
 - Academic research
- In all of these areas, there is a common strategy for success
- For example Consider that you want to start a company

First Example: Starting a Company:

Due Diligence

Idea → Company

Steps:

1. Invention
2. Size up the competition
3. Make sure the invention works
4. Make sure it's safe
5. Patent (secure intellectual property)
6. Figure out the best way to make it
7. Figure out how much to make
8. Is it the right thing to do?

Company
↓
Commercial Success

Diabetes
Phosphoproteome
Defined immuno-target
Develop a diagnostic kit
That feedback regulates
The amount of drug
delivered

This Course Covers These Strategic Issues

Second Example: The World is Struck by an Avian Influenza Pandemic:

Technical Diligence

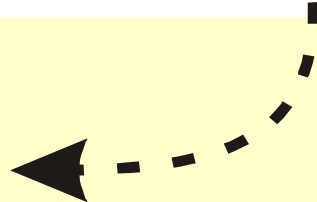
Idea



Company, CDC,
FDA, NGO ...

Steps:

1. Invention
2. Size up (the competition) options
3. Make sure invention works
4. Make sure it's safe
5. Patent (eventually this should become a business)
6. Figure out best way to make it
7. Figure out how much to make
8. Is it the right thing to do?



Crisis Averted
(May or may not be
A commercial success)

- Entire vaccine industry has a capacity of 1 B immunizations
- There are 6 B people on the planet

This Course Covers These Strategic Issues

Course History and Rationale

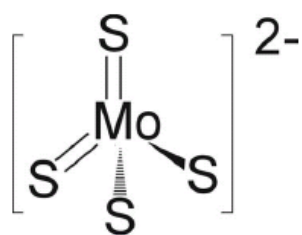
- The course (BE.105/5.22/10.02) originally focused on “due diligence” of biotech products that had recently entered the marketplace
- It was an exercise in reverse engineering
- Strong “analysis” component with some “design”
- MIT School of Engineering requires a “Design Course” (6.270, 2.007, ICE, etc.)
- The old course was re-engineered to focus on design of something new, rather than analysis of something already in existence
- We act as your consultants ... but the design is your own



This year, we have a tough one for you ... Inflammation underlies many diseases

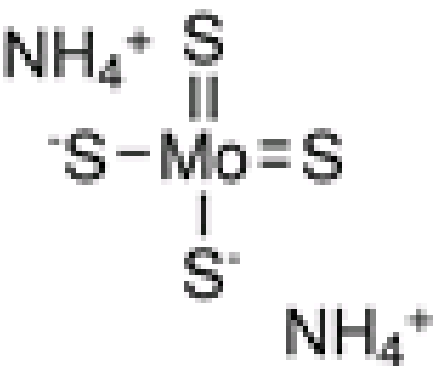
- Study and understand inflammation
- Use that knowledge to block disease progression
- Or, even better, prevent disease
- Maybe design a way to measure inflammation in vivo
- Perhaps you could even “deliver” inflammation to a target cell to kill it

Photo courtesy of [jpchan](#) on Flickr.



Pair of MRI images removed due to copyright restrictions.

Tetrathiomolybdate



A very brief example to show you how we think about design ...

Wilson's Disease and Bedlington Terriers: See Sternlieb, I., et al. "Inherited copper toxicity of the liver in Bedlington terriers." *Proc R Soc Med* 70, Suppl 3 (1977): 8-9. ([PDF](#))



How will you tackle your problem?

- Using a proven model of research management
- You will work in teams with a specific structure and hierarchy
- There is always a client ... a company, the government (NIH), a patron

ADL ... an early MIT spin-off



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*Arthur D. Little
MIT Chem. '84*

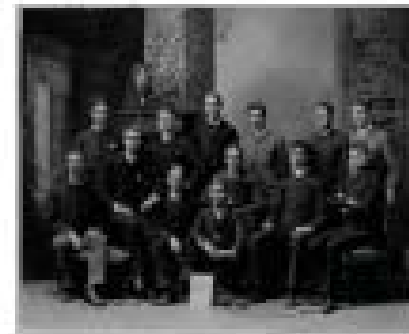
Arthur Dehon Little



Attended MIT 1881-1884. Studied chemistry; edited the student newspaper, *The Tech*.

Chairman of Alumni Association Publications Committee, which founded MIT's alumni magazine, *Technology Review*. First issue January 1899.

Member of MIT Corporation: Term member, 1912-1917 and 1918-1923; Life member, 1923-1935.



Staff of The Tech

[Larger image](#)

President of MIT Alumni Association, 1921-1922.

As a member and chairman of MIT Corporation Visiting Committees for Chemistry and Chemical Engineering, he was a strong advocate for advanced training in chemistry and its applications in many areas of industry. He was instrumental in the creation of the Chemical Engineering Practice School, the Research Laboratory of Applied Chemistry, and the Eastman Laboratories. His association with George Eastman proved advantageous in gaining Eastman's support for MIT.

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From the ADL, Inc. Centennial booklet, 1986:

[William H. Walker and Arthur D. Little] worked together to develop a curriculum for Chemical Engineering, the basis for a separate department established at MIT in 1920. The curriculum incorporated the concept of "unit operations," which Dr. Little first propounded in an address to the MIT Visiting Committee in 1916. The "unit operations" concept became the central organizing principle of large-scale chemical processes.

ADL-Matrix Structure of Our Consulting Group

Specialty Groups (Business Function)	Disease Groups (Industry Focus)							
	Diagnostic Technology		Role of Inflammation in Various Pathological States					
	Team 1	Team 2	Cancer 1	Cancer 2	Diabetes 1	Diabetes 2	Cardio-vascular Disease 1	Cardio-vascular Disease 2
Clinical description of disease; current treatments								
Design idea and rationale (two people)			<p>You, as consultants to our client, occupy one or more cells in the matrix structure</p>					
Mathematical modeling								
Proof of principle in vitro (single cell studies)								
Proof of principle in vivo (animal studies and clinical development)								
IP and company concept								

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Clinical description of disease; current treatments					Group			
Design idea and rationale (two people)								
Mathematical modeling								
Proof of principle in vitro (single cell studies)			Specialty Group					
Proof of principle in vivo (animal studies and clinical development)					Disease			
IP and company concept								

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Clinical description of disease; current treatments	Samiya		Maryelise		Group			
Design idea and rationale (two people)			Analiese				Yadir	
Mathematical modeling			Olga					Roli
Proof of principle in vitro (single cell studies)			Specialty Group					Jayanthi
Proof of principle in vivo (animal studies and clinical development)	Spenser				Disease		Kerry	
IP and company concept Impact projection							Stephanie	



Darrell



Forest

Now ... more granularity

- In February, the instructors will give background lectures on inflammation
- In February, we will form the groups and set up a Tuesday – Thursday rotation that will help groups (a) find their great idea, (b) trouble-shoot it and (c) flesh it out
 - Like Morpheus, we will place you in the matrix
 - Darrell developed a [Survey Monkey poll](#) to optimize happiness
- Now, let's look at the term schedule, and then a typical weekly schedule ...



The Term

Introduction to
Design Topic:
Inflammation

Cancer

Diabetes

Cardiovascular
Disease

Communications
Requirement

Regular
Lectures
(Background)
Darrell
John
Forest

February: TAs lead group-formation process

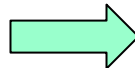
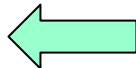
Students Present
Technical Papers

Exam

Disease Group
Design Pitches

March

Analysis

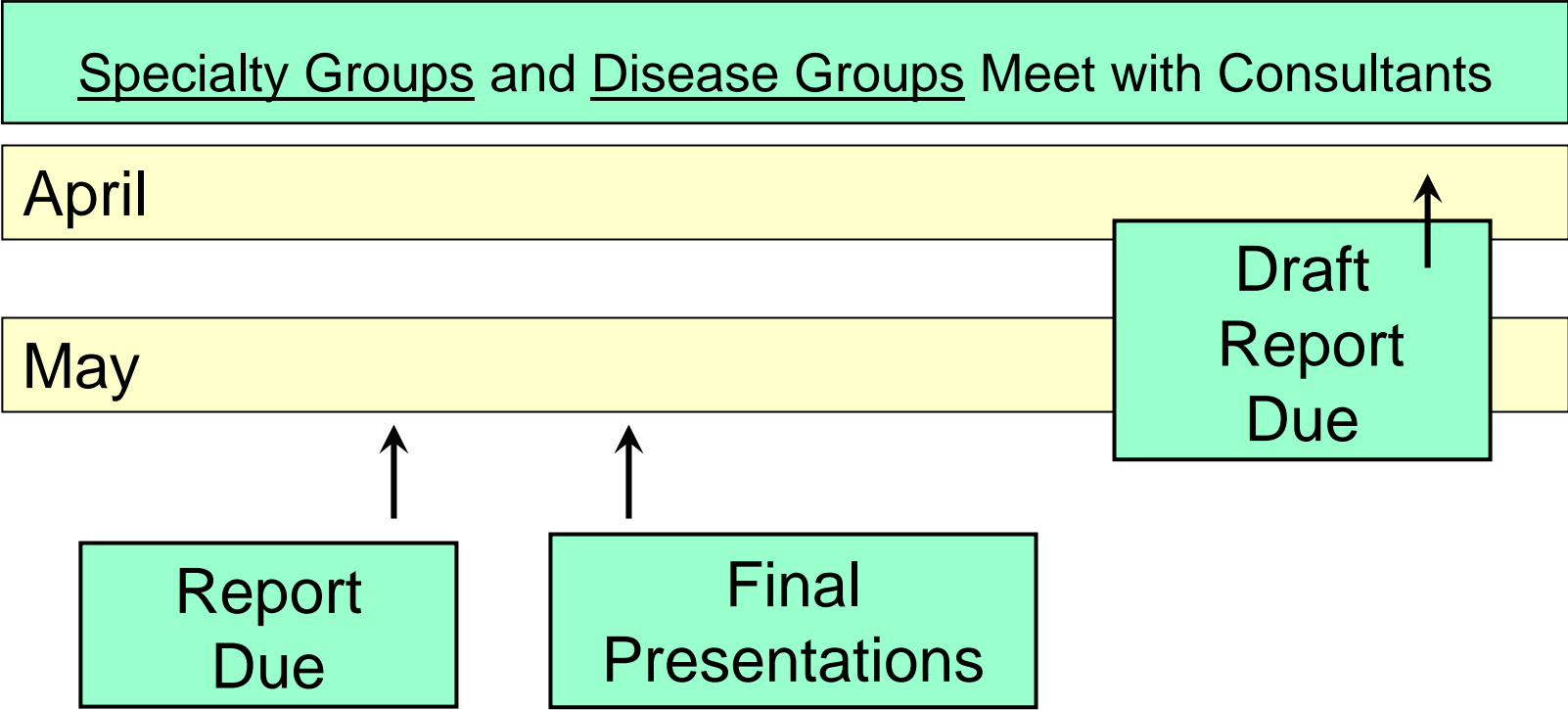


Design

March 9

Exam will cover the "technical papers"
The background lectures are meant to
help you understand those papers

The End of Term



The Term

Introduction to
Design Topic:
Inflammation

Cancer

Diabetes

Cardiovascular
Disease

Communications
Requirement

Regular
Lectures
(Background)
Darrell
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Forest

February: TAs lead group-formation process

Students Present
Technical Papers

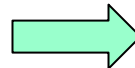
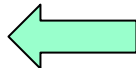
Exam

Disease Group
Design Pitches

March

Brugge

Analysis



Design

See Web Page

March 9

See Video

Tuesday 9-10 AM Recitations

Opportunity to Meet with Consultants

Course staff will make arrangements based upon student requests ...

Examples:

- RNA interference and siRNA delivery
- Drug targeting
- Drug carriers: liposomes, nanoparticles, dendrimers, ...
- Toxicity and side effects of existing chemotherapies
- Animal models of HIV and cancer: challenges, strengths, and weaknesses
- Immunotherapy strategies
- Patents and IP
- The challenge of FDA approval
- Dealing with peer review (responding to it formally)
- The steps one takes to start a company



Thursday 9-10 AM Recitations **Progress Reports Delivered to Staff**

Points:

- Meet every week
- Come to session equipped with:
 - Update on your progress toward the overall goal
 - List of questions for course staff
 - Answers to questions posed at previous meeting
 - Request for additional consultants for Tuesday Recitations

As we advance in the term (roughly after the Design Pitches), the course becomes a 10-12 “recitation” or workshop. We work intensively as a group to refine the design projects.

Lastly, a little more detail on the end of term

Specialty Groups a

April

May

Report
Due



- Thursday April 22: Paper draft due (~7 pages per student) to TAs and writing instructors
- Between 4/22 and 4/30 your paper will be pre-reviewed by Peers (other group), TAs, and CI-M instructors
- Draft will be returned ~ April 30
- Thursday May 6 Final paper due (with written point by point response to peer review)
- Wednesday May 12 (7 pm) Final presentations to experts (faculty, local business people); this event will be preceded by dinner and held at Simmons Hall. This meeting is mandatory.

Group 4: Diabetes 1

Group 5: Diabetes 2

Group 6:



Final Presentation with Client

- MIT faculty in BE will examine your work
- Selected industry members will be invited
- 20.380 Alumni
- Future 20.380 students

The “Client” Roster from May, 2009

- Professor Forest White, BE, MIT
- Dr. Ganesh Venkataraman, Founder, CSO and SVP of Momenta Pharmaceuticals
- Dr. Maryann Timins, Senior Scientist, Momenta
- Dr. Peter Rye, Science-business Interface, BioTrove
- Dr. Hector Hernandez, Department of Civil and Environmental Engineering, MIT
- Dr. James Delaney, Research Scientist, Parasol Therapeutics



20.380 Class of 2009

Several slides of 2009 class presentations removed due to privacy and copyright restrictions.

Let's Look at the Syllabus

- Course Requirements
- Recitations with Your TAs and Course Staff Tues Thurs at 9 AM (have coffee with us as early as 8:30)
- Grading
 - Technical
 - CI-M

Grading

- Examination on technical papers (March 9) (15%)
- Technical paper presentation (10%)
- Design pitch and interim progress reports of group ideas in Recitations (25%)
- Peer review of another group's work (10%)
- Class participation (attendance is mandatory) (10%)
- Final written report (20%)
 - This can be a grant proposal
 - Or a business plan (due diligence document)
- Final presentation to faculty on May 13, 2010 (10%)



Introduction of TA Staff

Jesse Shapiro and Peter
DeMuth

Jesse

- BSc Biology/MSc Integrative Bioscience
- Current 5th-year PhD student in CSBi
- Advisor: Eric Alm
- Research interests: microbial evolution & genomics; human-microbe interactions

Peter

- B.S. Chemical Engineering
- B.S Biochemistry
- Current 2nd-year PhD student in BE
- Advisor: Darrell Irvine
- Research interests: materials development for transdermal vaccination


Teaching Staff Challenges

- Student absences
 - Class attendance is required (because it is a team-oriented design course)
 - Some of you will be missing a class a week owing to interviews
 - This problem lasts until Spring Break
 - We'll be understanding but you have to keep up with your work
 - Don't let your team down
 - Don't flunk the exam
 - Let the TAs know if you are going to miss class
- Computer use in class
 - OK if you are looking up material relevant to the course
 - Not OK if you are checking your e-mail, Facebook, Twitter
 - We need your full attention – many companies now prohibit Blackberrys in meetings



Introduction of CI-M Staff

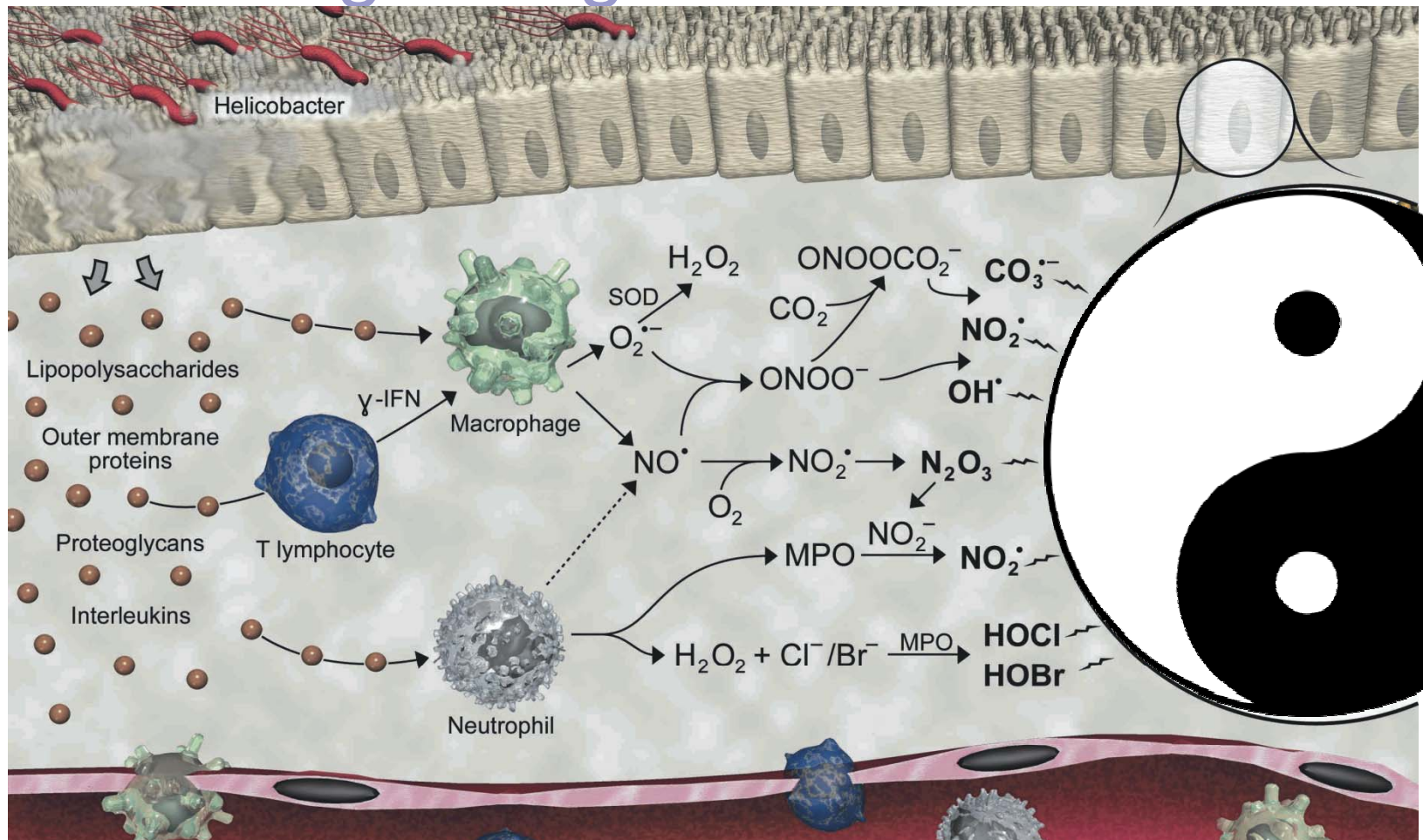
Definition of expectations and
grading policies



The problems we shall tackle in this year ... brainstorm a bit on each one

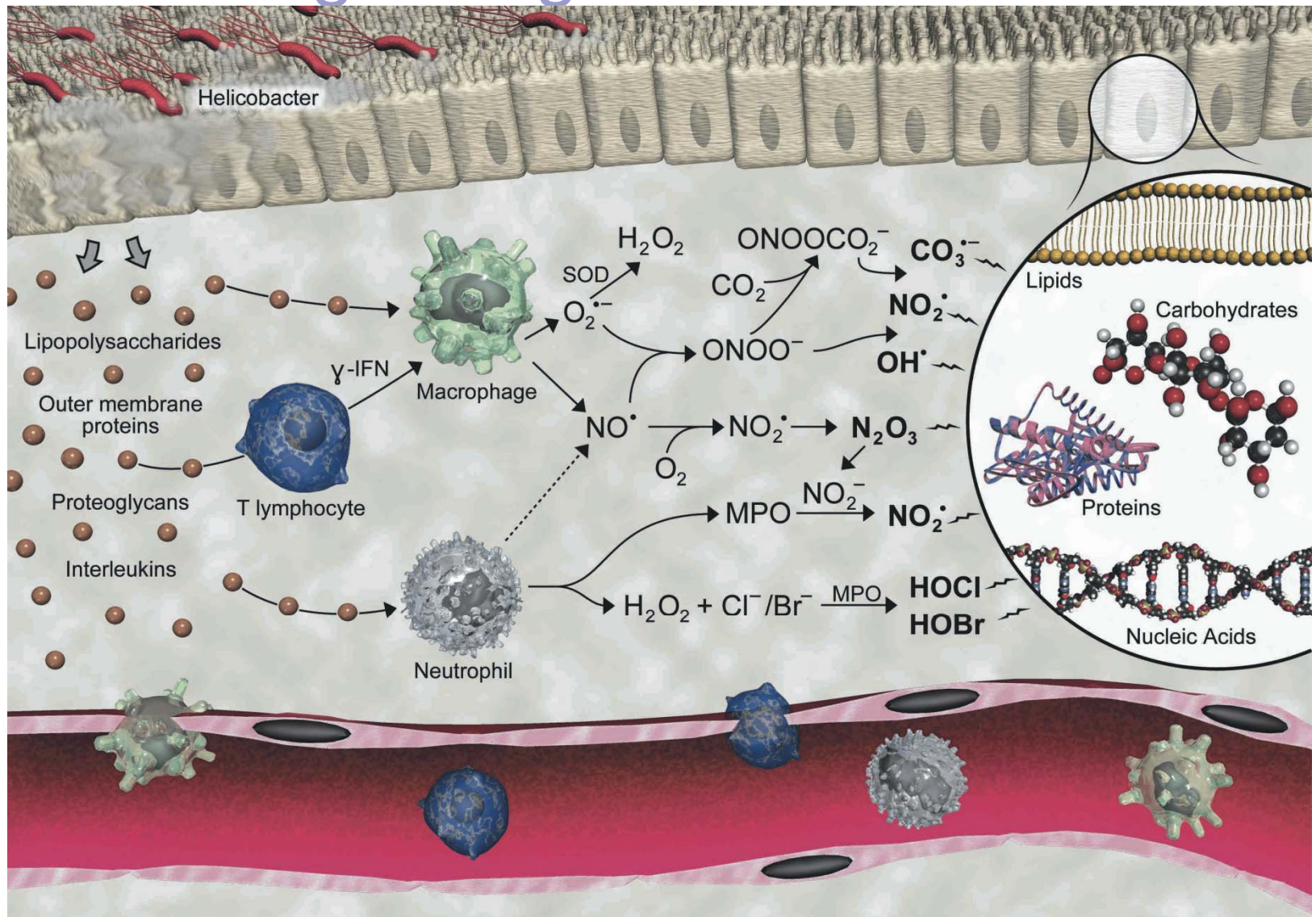
- Diabetes and inflammation
- Cancer and inflammation
- Cardiovascular disease and inflammation

Design Target: Inflammation



Yin-Yang --- Inflammation protects us from invading organisms but the cost is an excess of disease caused by collateral damage

Design Target: Inflammation



Cancer, Diabetes, Cardiovascular Disease

2007 Estimated US Cancer Deaths

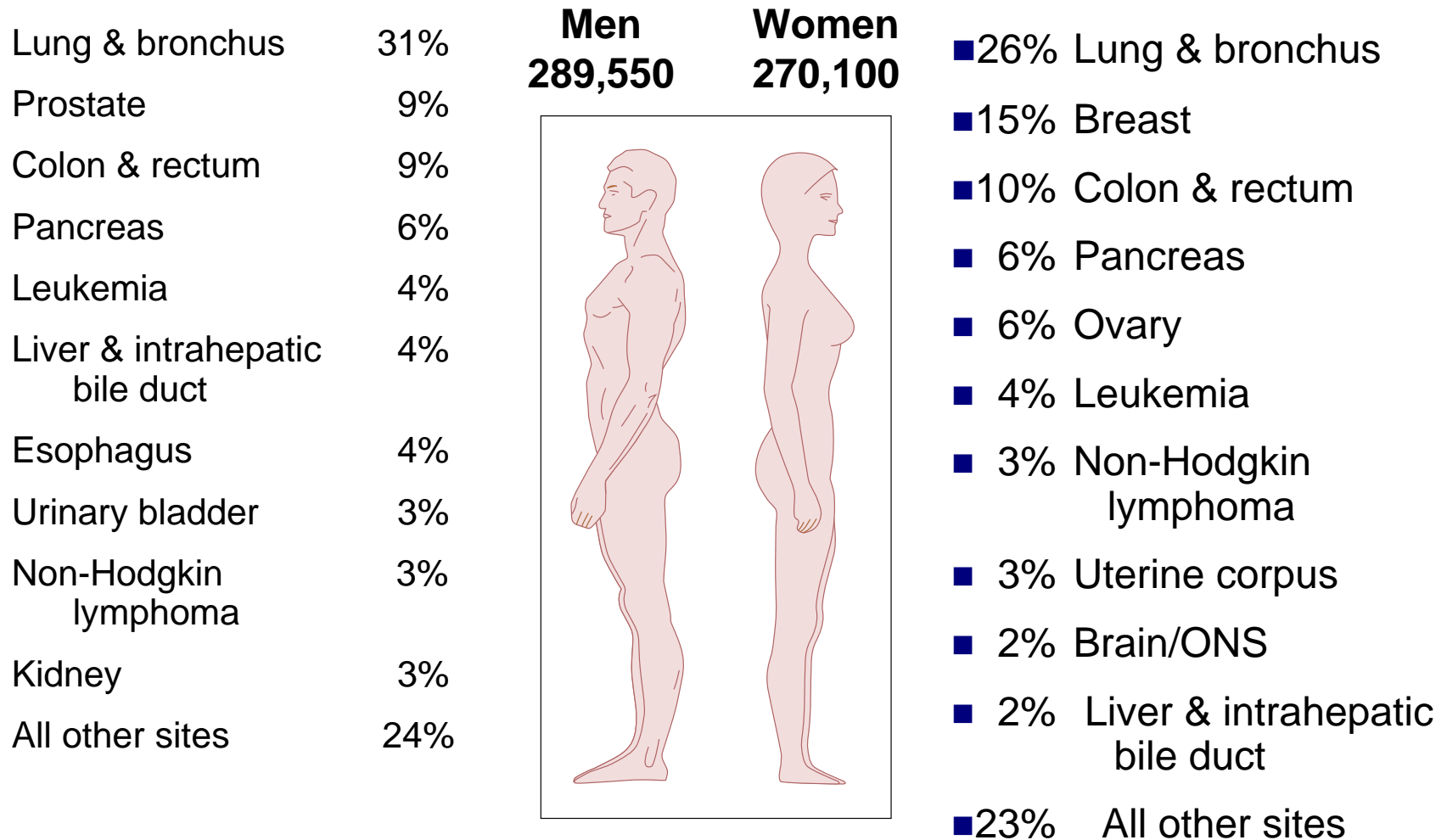


Figure by MIT OpenCourseWare.

ONS=Other nervous system.

Source: American Cancer Society, 2007.

Progression of Normal Cells to Cancer Cells (Liver = Example)

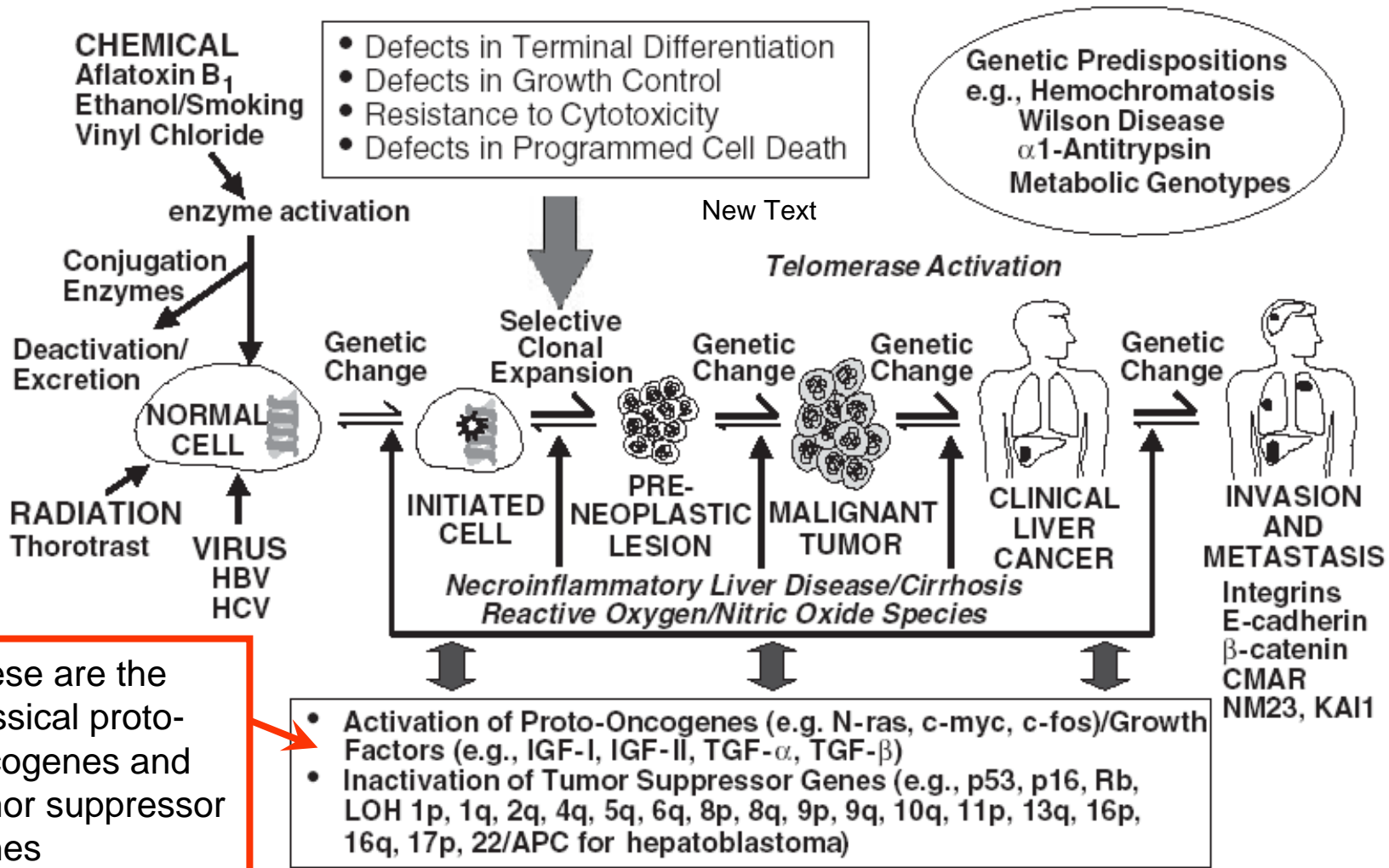


FIGURE 2. Multistage hepatocarcinogenesis. (CMAR, cellular adhesion regulatory molecule; HBV, hepatitis B virus; HCV, hepatitis C virus; IGF-I, insulin-like growth factor-I; IGF-II, insulin-like growth factor-II; LOH, loss of heterozygosity; TGF- α , transforming growth factor α ; TGF- β , transforming growth factor β).

Progression of Normal Cells to Cancer Cells (Liver = Example)

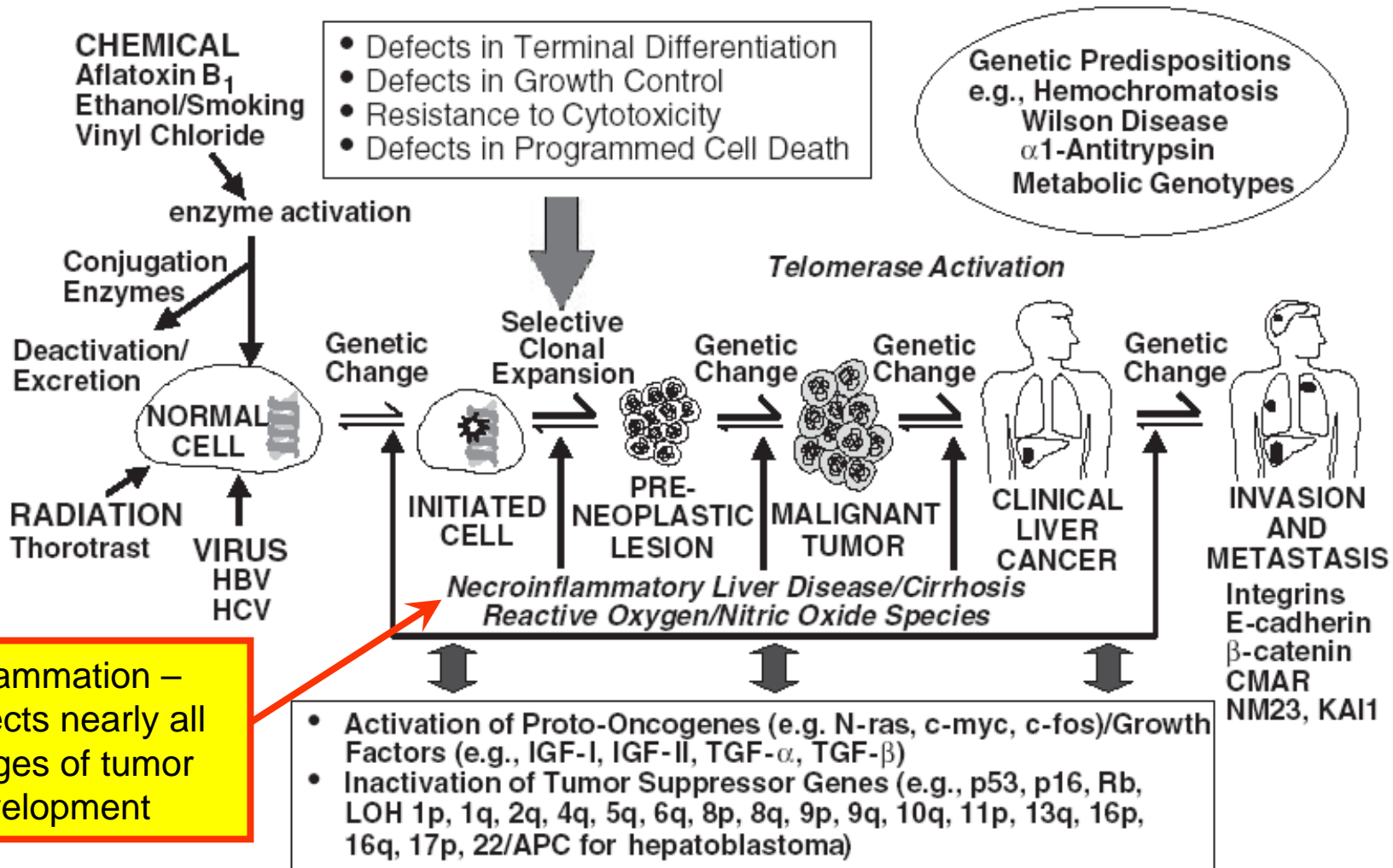


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Reprinted by permission from Macmillan Publishers Ltd: Oncogene. Source: Hussain, S. P., et al. "TP53 mutations and hepatocellular carcinoma: insights into the etiology and pathogenesis of liver cancer." Oncogene 26 (2007): 2166-2176. © 2007.

Design is Important

8:30-10 AM, Tues and Thurs



We want to meet with you in a relaxed setting

Design is Important



For OCW, student faces covered for privacy reasons.

Collegiality at 8:30 AM

Design is Important

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and <http://www.flickr.com/photos/aboutdesign/3590660324/>

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20.380J / 5.22J Biological Engineering Design
Spring 2010

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