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Spring 2019  
E62-276

## The Science and Business of Biotechnology

This course focuses on early-stage biotechnology companies, with particular emphasis on understanding the underlying science, technology, and disease targets—together with the application of novel business structures and financing methods—to facilitate drug discovery, clinical development, and greater patient access to new but potentially high-cost therapies.

Current research is enhancing our understanding of the genetic, molecular, and cellular bases of many human diseases, and is leading to many new types of biotherapeutics that we will cover in this course, including recombinant therapeutic proteins; monoclonal antibodies and antibody drug conjugates; cancer immunotherapies, replacement cells and genetically engineered cells; and nucleic acid and gene therapies. Translating these discoveries into drugs and diagnostics increasingly requires the establishment of for-profit companies, but funding for early-stage development of novel therapies is becoming scarcer, especially for therapeutics for “rare” diseases that affect small populations. The dearth of funding for early-stage biotherapeutics companies in the so-called “Valley of Death” can be attributed to several factors, but a common thread is increasing financial risks in the biopharma industry and greater uncertainty surrounding the scientific, medical, economic, political, and academic environments within the biomedical ecosystem. Increasing risk and uncertainty inevitably leads to an outflow of capital as investors and other stakeholders seek more attractive opportunities in other industries.

By applying financial techniques such as portfolio theory, securitization, and derivative securities to biomedical contexts, more efficient business and funding structures can be developed to reduce financial risks, lower the cost of capital, and bring more life-saving therapies to patients faster. Thus this course will also cover basic financial analysis for the life-sciences professional; the historical financial risks and returns of the biotech and pharmaceutical industries; the evaluation of the science and business potential as well as the mechanics of financing biotech startups; capital budgeting for biopharmaceutical companies; and applications of financial engineering in drug royalty investment companies, biomedical megafunds, drug approval swaps, and life sciences investment banking.

The target audience for this course includes both Sloan and life-sciences graduate students who are interested in careers in the healthcare industry.

### Pre-/Co-requisite

This course requires that Sloan students have either taken, or are concurrently taking, 15.401 Managerial Finance. Life-sciences students must have a basic background in cellular and molecular biology. These requirements can be waived by permission of instructor.

### Class Schedule

The class meets once per week: T 4:30–7:30pm, E62-276. During the first half of the semester, the classes will be mainly lectures; during the second half of the semester, classes will consist of lectures for the first two hours and a guest speaker for the last hour.

## Recitations

The TAs, Chi Heem Wong and Catherine (Kate) Koch, will hold recitations on Thursdays, 4:00–6:00pm, E62–233. Recitations will primarily focus on teaching core concepts in molecular and cellular biology to Sloan students, and teaching basic principles of finance for science and engineering students. Class material will be reviewed and additional applications and exercises presented. Questions should be directed to [chiheem@mit.edu](mailto:chiheem@mit.edu) and [kkoch@mit.edu](mailto:kkoch@mit.edu).

## Course Website

The primary course website is <https://mit.instructure.com/courses/1109> and all teaching materials except online assignments will be posted on this site, including announcements, TA office hours, lecture notes, readings, handouts, and data. Cases can be downloaded at <http://study.net> and the online assignments, and their solutions, can be found under 15.480 on the MITx website <https://lms.mitx.mit.edu/courses>.

## Office Hours

The course instructors and TAs will also hold regular office hours, and the times and locations will be announced on the course website.

## Administrative Assistants

Course Admin: Crystal Myler, E62–611, (617) 715–4840, [cmyle@mit.edu](mailto:cmyle@mit.edu)

For Prof. Lo: Crystal Myler (see above)

For Prof. Lodish: Mary Anne Donovan, [donovan@wi.mit.edu](mailto:donovan@wi.mit.edu)

## Course Requirements and Grading

Course requirements include regular attendance and participation in class which requires having read the assigned chapters in the textbook and having viewed the biology videos prior to coming to class and being prepared to discuss them, which will be assessed via short pre-lecture quizzes (5%). In addition, there are nine problem sets / case studies (60%, the lowest score dropped), and one group project due before the end of the semester (35% = 30% for project deliverables + 5% for peer evaluation). There is no final examination for the class.

The group project involves choosing one of the following options based on the specific interests of your group: (1) prepare a business plan for a biotech startup; (2) perform a financial analysis of a biotech or pharma company as an investment or acquisition target; (3) propose a new funding structure for an unmet medical need, e.g., vaccines for infectious diseases, gene therapies, a clinic for terminally ill patients, healthcare loans for gene therapies, etc.; or (4) a project of your choosing with prior written approval from the instructor. The final deliverable will be a max 5,000-word research paper, a 5-slide presentation, and a 5-minute video presenting your project as if to an investor or client. **Groups will be selected based on their video to present to a panel of biopharma industry experts during the last class, and the most compelling projects will receive awards.**

## Course Materials

- **Class Notes and Recitation Notes.** Notes including the readings entitled *Healthcare Finance* will be available on the course website.
- **Research Articles.** Research articles will be made available on the course website.
- **Textbook.** Lodish et al., *Molecular Cell Biology*, 8th ed. 2016.

### **Additional Recommended Readings**

S. Mukherjee, *The Emperor of All Maladies*, 2010.

- Pulitzer-prize-winning “biography” of cancer, which is a fascinating introduction to one of the most important motivations for this course.

L. Friedhoff, *New Drugs: An Insider’s Guide to the FDA’s New Drug Approval Process*, 2009.

- A very concise exposition of the process of getting a drug approved by the FDA, written by an MD/PhD and 30-year veteran of the pharma industry who headed teams that developed and received FDA approval for six new drugs, including the blockbusters Aricept and Aciphex.

### **Sloan Values**

You are responsible for upholding Sloan’s code of conduct, which mandates zero tolerance for cheating and plagiarism. For more details on Sloan’s academic policies, please read the document ***Classroom Values in Practice*** which is available on the course website.

## Class and Assignments Schedule<sup>1</sup>

Class	Topic
L1: 2/5	<p><b>Introduction to Drug Development; New Types of Biotherapeutics</b></p> <ul style="list-style-type: none"><li>▪ Small molecule drugs</li><li>▪ Recombinant therapeutic proteins</li><li>▪ Improving recombinant protein function</li></ul> <p><b>Introduction to Healthcare Finance</b></p> <ul style="list-style-type: none"><li>▪ Motivation for healthcare finance</li><li>▪ A taxonomy of the biomedical ecosystem</li><li>▪ Crash course in financial analysis</li></ul> <p><b>Required Readings</b></p> <ul style="list-style-type: none"><li>▪ HFin: Chapters 1 (Introduction and Overview) and 2 (Present Value Relations and Valuation)</li><li>▪ DNA Cloning: <a href="https://www.khanacademy.org/science/biology/biotech-dna-technology/dna-cloning-tutorial/a/overview-dna-cloning">https://www.khanacademy.org/science/biology/biotech-dna-technology/dna-cloning-tutorial/a/overview-dna-cloning</a></li></ul> <p><b>Required Videos</b></p> <ul style="list-style-type: none"><li>▪ DNA Cloning and recombinant DNA<ul style="list-style-type: none"><li>○ <a href="https://www.youtube.com/watch?v=5ffl-00YVQU">https://www.youtube.com/watch?v=5ffl-00YVQU</a></li></ul></li><li>▪ The Birth of Modern Biomanufacturing: the Genzyme story<ul style="list-style-type: none"><li>○ <a href="https://www.youtube.com/watch?v=Sdbezd16xTU">https://www.youtube.com/watch?v=Sdbezd16xTU</a></li></ul></li><li>▪ Post Translational Modifications<ul style="list-style-type: none"><li>○ <a href="https://www.youtube.com/watch?v=VFQ41isfAa8">https://www.youtube.com/watch?v=VFQ41isfAa8</a></li></ul></li></ul> <p><b>Finance Advanced Readings</b></p> <ul style="list-style-type: none"><li>▪ Thomas, D. and Wessel, C. 2018. <i>Emerging Therapeutic Company Investment and Deal Trends 2008–2017</i>. Washington, DC: BIO.</li><li>▪ Thakor, R., Anaya, N., Zhang, Y., Vilanilam, C., Siah, K., Wong, C., Lo, A. 2017. Just how good an investment is the biopharmaceutical sector?, <i>Nature Biotechnology</i> 35, 1149–1157.</li></ul> <p><b>Biology Advanced Readings</b></p> <ul style="list-style-type: none"><li>▪ MCB pages 585–592, 601–608, and 631–658: Synthesis and processing of secreted proteins</li><li>▪ MCB pages 249–253: Production of recombinant proteins</li></ul> <p><b>Optional Resources</b></p> <ul style="list-style-type: none"><li>▪ Leader, B. et al. 2008. Protein therapeutics: a summary and pharmacological classification. <i>Nature Reviews Drug Discovery</i></li><li>▪ Opar, A. 2011. Excitement mounts for first disease-modifying cystic fibrosis drugs. <i>Nature Reviews Drug Discovery</i> Kaplan, R. and S. Hood.</li></ul>

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<sup>1</sup> Please note that the class and assignments schedule is approximate and we reserve the right to make changes depending on the interests and background of the participants. **Also, guest speakers have not all been confirmed.** Most readings, including those from *Healthcare Finance* (HFin), will be made available on Canvas. Readings designated “MCB” are from Lodish et al., *Molecular Cell Biology*, 8th ed.

2010. Bob Beall at the Cystic Fibrosis Foundation. Harvard Business School.

R1: 2/7 *Present value relations and valuation*  
*Basic concepts in biology and overview of recombinant proteins*

**L2: 2/12 Adeno Associated Viral (AAV) Vectors and Gene Therapy**

- Hemophilia
- Hereditary Blindness
- Spinal Muscular Atrophy

**Financial Analysis for the Life Sciences Professional, Part 1**

- Capital budgeting techniques
- Determining the appropriate risk-adjusted cost of capital

**Required Readings**

- HFin: Chapter 3 (Capital Budgeting)
- Dunbar, C. 2018. Gene therapy comes of age (An excellent review of recent advances in gene therapy). *Science* 359, 175 (2018) and *Science* 359, ean4672 (2018) pp1, 2 and pp 6,7
- K. Talbot and E.F. Tizzano. 2017. The clinical landscape for SMA in a new therapeutic era. *Gene Therapy* 24, 529–533
- J. Kaiser. 2017. A Second Chance: A neuron-targeting gene therapy delivered into the blood saves infants with a deadly spinal disease—and boosts an entire field. *Science* 358: 582

**Required videos:**

- Gene Therapy Explained:  
<https://www.youtube.com/watch?v=xOQFJJOBGM0>
- SMA Type 1 Gene Therapy:  
[https://www.youtube.com/watch?v=iBmyXr\\_o1hU](https://www.youtube.com/watch?v=iBmyXr_o1hU)
- Gene Therapy: <https://www.youtube.com/watch?v=znZVsNBkrQs>

**Assignments Due**

- Pre-lecture readings quiz 1 and 2
- Problem set 1: Present value relations

**Finance Advanced Readings**

- Cockburn, I. and Lerner, J. 2009. The cost of capital for early-stage biotechnology ventures.
- Harrington, S. 2012. Cost of capital for pharmaceutical, biotechnology, and medical device firms, in Danzon, P. and Nicholson, S. (eds.), *The Oxford Handbook of the Economics of the Biopharmaceutical Industry*, pp. 75–99. New York: Oxford University Press.

**Biology Advanced Readings**

- MCB page 494: Cystic Fibrosis
- MCB pages 694–699: Vision

## Optional Resources

- How stuff works gene therapy introduction:  
<https://science.howstuffworks.com/life/genetic/gene-therapy.htm>
- Lee, H. and Lotery, A. 2017. Gene therapy for *RPE65*-mediated inherited retinal dystrophy completes phase 3. *Lancet*
- Lillicrap, D. 2017. FIX It in One Go: Enhanced Factor IX Gene Therapy for Hemophilia B. *Cell*

R2: 2/14 *Capital budgeting and cost of capital*  
*Introduction to gene therapy: viruses*

2/19 *MONDAY SCHEDULE (NO LECTURE)*

## L3: 2/26 **Gene Therapy: Retroviral Vectors**

- Severe combined immune deficiency
- Wiscott Aldrich Syndrome and HIV-based vectors

## **Financial Analysis for the Life Sciences Professional 2**

- Pricing stocks and bonds
- Buying cures vs. renting health

**Guest Speaker:** Jodi Cook, former COO of Agilis Biotherapeutics

## **Required Readings**

- HFin: Chapter 6.1 – 6.2 (Risk, Reward)
- Dunbar, C. 2018. Gene therapy comes of age (An excellent review of recent advances in gene therapy). *Science* 359, 175 (2018) and *Science* 359, eaan4672 (2018) pp1, 2 and pp 6,

## **Required videos:**

- **Gene therapy retroviruses:**
  - <https://www.youtube.com/watch?v=v9nkcOsaWa4>
- **Gene Therapy:**
  - <https://www.youtube.com/watch?v=znZVsNBkrQs>

## **Assignments Due**

- Pre-lecture readings quiz 3
- Problem set 2: Capital budgeting

## **Finance Advanced Readings**

- Hampson, G., Towse, A., Pearson, S., Dreitlein, W., Henshall, C. 2018. Gene therapy: evidence, value and affordability in the US health care system. *Journal of Comparative Effectiveness Research* 7, 15–28.
- Montazerhodjat, V., Weinstock, D., and Lo, A. 2016. Buying cures vs. renting health: Financing health care with consumer loans. *Sci. Trans. Med.* 8, 327ps6.

## **Biology Advanced Readings**

- MCB pages 212–218: Virus molecular biology

- MCB page 252: Retroviral vectors
- MCB pages 316–318: Retrovirus molecular biology
- MCB pages 666–668: Formation of retrovirus particles
- Hacein-Bey-Abina, S., et.al. 2014 A Modified  $\gamma$ -Retrovirus Vector for X-Linked Severe Combined Immunodeficiency *New England Journal of Medicine* 15: 1407 – 1417

### Optional Resources

- L. Geddes. 2013. Bubble kid' success puts gene therapy back on track. *New Scientist*
- R. Herzog et al. 2010. Two Decades of Clinical Gene Therapy—Success Is Finally Mounting. *Discov. Med.* 9:105–111
- How stuff works gene therapy introduction:  
<https://science.howstuffworks.com/life/genetic/gene-therapy.htm>

R3: 2/28     *Pricing stocks, bonds, and mortgages*  
*Introduction to gene therapy: logistics and applications*

### L4: 3/5     Developing Therapeutics

- Overview of the drug development process
- Randomized clinical trial design
- Size, power, and cost

### Planning and Executing Clinical Trials for Lentiviral Gene Therapy: Hereditary Anemias as a Global Problem

- Beta thalassemia
- Sickle Cell Disease

**Guest speaker:** Erica Esrick, Attending Physician, Dana-Farber/Boston Children's Hospital

### Required Readings

- HFin: Chapter 7 (Drug Development and Clinical Trials), only 7.1–3.
- Kingwell, K. 2016 Sickle cell solutions in sight *Nature Reviews Drug Discovery* 15: 593
- Gene therapy in a patient with sickle cell disease:  
<https://www.nejm.org/doi/full/10.1056/nejmoa1609677>

### Assignments Due

- Pre-lecture readings quiz 4
- Problem set 3: Pricing stocks, bonds, and mortgages

### Finance Advanced Readings

- Scannell, J., et al. 2012. Diagnosing the decline in pharmaceutical R&D efficiency. *Nature Reviews Drug Discovery* 11, 191–200.

### Biology Advanced Readings

- MCB pages 994–996: Formation of blood cells
- McCavit,T., 2012 Sickle Cell Disease. *Pediatrics in Review* 33: 195

### Optional Resources:

- Ellimoottil, C., Vijan, S. and Flanigan, R. 2015. A primer on clinical trial design. *Urologic Oncology* 33, 116–121.
- Isakov, L., Lo, A. and Montazerhodjat, V. 2017. Is the FDA too conservative or too aggressive?: A Bayesian decision analysis of clinical trial design. Forthcoming in *Journal of Econometrics*.
- Montazerhodjat, V., Chaudhuri, S., Sargent, D. and Lo, A. 2017. Use of Bayesian Decision Analysis to Minimize Harm in Patient-Centered Randomized Clinical Trials in Oncology”  
<https://jamanetwork.com/journals/jamaoncology/fullarticle/2618072>
- Chaudhuri, S., Ho, M., Irony, T., Sheldon, M. and Lo, A. 2017. Patient-centered clinical trials. *Drug Discovery Today*

R4: 3/7

*Clinical trial design*

*Sickle Cell Anemia / Beta Thalassemia overview and approaches to treatment*

L5: 3/12

### Nucleic Acid Therapies

- shRNAs causing degradation of target messenger RNA
- Oligonucleotides that affect splicing of pre-mRNA
- Duchenne Muscular Dystrophy
- Spinal Muscular Atrophy

### Portfolio Theory for Biomedical Assets

- Mean-variance portfolio optimization
- The role of correlation in de-risking biomedical assets
- Mini-case: Orphan drug portfolios

**Guest Speaker:** Ilan Ganot, Founder and CEO, Solid Biosciences

### Required Readings

- R. Kole and A. Krieg. 2015. Exon skipping therapy for Duchenne muscular dystrophy. *Advanced Drug Delivery Reviews* 87:104
- Have antisense oligonucleotides hit their stride? *Chem Eng News* 2018  
<https://cen.acs.org/content/cen/articles/96/i45/antisense-oligonucleotides-hit-stride.html>
- Drug treatment targets mutant proteins to stop neurodegenerative diseases <http://theconversation.com/drug-treatment-targets-mutant-proteins-to-stop-neurodegenerative-diseases-106100>
- Novartis gains priority review for SMA gene therapy as investors grapple with sticker shock: <https://endpts.com/novartis-gains-priority-review-for-sma-gene-therapy-as-investors-grapple-with-sticker-shock/>
- Chapter 6.3 (Cost of Capital)

### Assignments Due

- Pre-lecture readings quiz 5
- Problem set 4: Clinical trials



### Finance Advanced Readings

- Fagnan, D., Yang, N., McKew, J., Lo, A. 2015. Financing translation: Analysis of the NCATS rare-diseases portfolio. *Science Translational Medicine* 7, 276ps3.
- Kim, E. and Lo, A. 2016. Business models to cure rare disease: A case study of Solid Biosciences. *Journal of Investment Management* 14, 87–101.

### Biology Advanced Readings

- MCB pages 419–434
- MCB pages 445–450
- Antisense oligonucleotides the next frontier for treatment of neurological disorders:  
<https://www.nature.com/articles/nrneurol.2017.148>

### Optional Resources

- Giaccotto, C. , Golec, J. and Vernon, J. 2011. New estimates of the cost of capital for pharmaceutical firms. *Journal of Corporate Finance* 17, 526–540
- Paradise, J. 2016. A profile of bio-pharma consolidation activity. *Annals of Health Law* 25, 34–61
- Khan Academy: Intro to gene expression, the genetic code, and nucleic acids: <https://www.khanacademy.org/science/biology/gene-expression-central-dogma/central-dogma-transcription/a/intro-to-gene-expression-central-dogma>
- Antisense gene therapy: [http://web.stanford.edu/group/hopes/cgi-bin/hopes\\_test/antisense-gene-therapy/](http://web.stanford.edu/group/hopes/cgi-bin/hopes_test/antisense-gene-therapy/)
- RNAi: [http://web.stanford.edu/group/hopes/cgi-bin/hopes\\_test/?s=rna+interference](http://web.stanford.edu/group/hopes/cgi-bin/hopes_test/?s=rna+interference)

R5: 3/14 *Diversification and portfolio optimization*  
*Nucleic acids overview: therapeutic applications and mechanisms of action*

3/19 *SIP WEEK*

3/26 *SPRING BREAK*

### L6: 4/2 **Gene Editing**

- Zinc finger nucleases
- TALENs
- CRISPR and its modifications

### Valuation of Life Sciences Assets

- Valuing basic scientific research, patents, royalties, licensing deals, and milestone payments, and drug development projects as risky cash flows
- Applications of decision trees, real options, and simulations

**Guest Speaker:** Andrew Hack, Bain Capital (Former CFO, Editas)

### Required Readings

- HFin: Chapter 8 (Decision Trees and Real Options)
- CRISPR in 2018: Coming to a Human Near You: <https://www.technologyreview.com/s/609722/crispr-in-2018-coming-to-a-human-near-you/>
- Chinese Scientist Claims to Use CRISPR to Make First Genetically Edited Babies: <https://www.nytimes.com/2018/11/26/health/gene-editing-babies-china.html>

### Required Videos

- CRISPR
  - <https://www.youtube.com/watch?v=4YKFW2KZA5o>

### Assignments Due

- Pre-lecture readings quiz 6
- Problem set 5: The CAPM and diversification

### Finance Advanced Readings

- Lynch, J. and Shockley, R. 2016. Valuation of a developmental drug as a real option. *Journal of Applied Corporate Finance*.

### Biology Advanced Readings

- MCB pages 259–268: Inactivating genes and gene editing
- Komor, A. et. al., Editing the Genome Without Double-Stranded DNA Breaks *ACS Chem. Biol.*, 2018, 13 (2), pp 383–388

### Optional Resources

- Feldman, R. 2016. The CRISPR revolution: What editing human DNA reveals about the patent system's DNA. *UCLA Law Review Discourse* 64, 392–410

R6: 4/4

*Decision trees and real options*

*Approaches to gene editing and potential applications of CRISPR-Cas9 system*

L7: 4/9

### Antibody Generation

- Gentle introduction to the immune system
- Vaccine Development
- Antibody structure
- Generation of antibody diversity

### Biotech Venture Capital and New Business Models

- Legal and financial structure of biotech VC funds, typical deal structures
- Valuation models for biopharma companies

**Guest Speaker:** Avind Gupta, Partner and Alex Kopelyan, Program Director and Partner, IndieBio

### Required Readings

- HFin: Chapter 9 (Biotech Venture Capital)

- Lo A. and Narahariseti, S. 2014. New Financing Methods in the Biopharma Industry: A Case Study of Royalty Pharma. *Journal of Investment Management*, 12, 4–19.
- Immunology Overview Handout by Kate Koch

### Required Videos

- Immunology wars: A billion antibodies
  - <https://www.youtube.com/watch?v=Na-Zc-xWCLE>
- Camelid single domain nanobodies
  - <https://www.youtube.com/watch?v=rXUyJTzb0cc>

### Assignments Due

- Pre-lecture readings quiz 7
- Problem set 6: Decision trees and real options

### Finance Advanced Readings

- Lo, A. 2017. “Quantifying the Impact of Impact Investing,” pre-print, MIT Laboratory for Financial Engineering
- Locust Walk Partners. 2017. *Biopharma Valuation Analysis*. Boston, MA: Locust Walk Partners.

### Biology Advanced Readings

- MCB pages 1089–1103: Structure of antibodies and generation of antibody diversity

### Optional Resources

- Guo, R., Lev, B. and Zhou, N. 2005. The valuation of biotech IPOs. *Journal of Accounting, Auditing and Finance*
- Forman, S., Lo, A., Shilling, M. and Sweeney, G. 2015. Funding translational medicine via public markets: The business development company. *Journal of Investment Management*

R7: 4/11 *No recitation for finance, will be available for consultation  
Immunology overview: B-cells, antibodies, and vaccines*

4/16 *PATRIOT'S DAY*

### L8: 4/23 Monoclonal Antibodies

- Generation of mouse and human monoclonal antibodies
- Monoclonal antibodies targeting Tumor Necrosis Factor alpha (TNF $\alpha$ )
- Monoclonal antibodies targeting specific tumor cells
- Antibody drug conjugates

### Megafunds and Cancer

- Introduction to securitization and biomedical megafunds
- Hollywood, project-based organizations, and slate financing

**Guest Speaker:** Pablo Legorreta, Royalty Pharma

### Required Readings

- R. Zolot et al. 2013. Antibody–drug conjugates. *Nature Reviews Drug Discovery*
- Lo, A. and Pisano, G. 2015. Lessons from Hollywood: A New Approach to Funding R&D. *MIT Sloan Management Review*
- HFin: Chapter 11 (Securitization)

### Required Videos

- Immunology wars: Monoclonal antibodies
  - <https://www.youtube.com/watch?v=5AXApBbj1ps>
- Antibody drug conjugate
  - <https://www.youtube.com/watch?v=08q2Th3GQ5w>

### Assignments Due

- Pre-lecture readings quiz 8
- Problem set 7: Biotech venture capital

### Finance Advanced Readings

- Fernandez, J.-M., Stein, R. and Lo, A. 2012. Commercializing biomedical research through securitization techniques. *Nature Biotechnology*, 30, 964–975.
- Montazerhodjat, V., Frishkopf, J. and Lo, A. 2016. Financing drug discovery via dynamic leverage. *Drug Discovery Today*, 21, 410–414.

### Biology Advanced Readings

- MCB pages 135–136: Production of monoclonal antibodies
- MCB page 1131: The immune system defends against cancer

### Optional Resources

- Fagnan, D., Yang, N., McKew, J. and Lo, A. 2015. Financing translation: Analysis of the NCATS rare-diseases portfolio. *Science Translational Medicine*
- Lo, A., Ho, C., Cummings, J. and Kosik, K. 2014. Parallel discovery of Alzheimer's therapeutics. *Science Translational Medicine*
- Hull, J., Lo, A. and Stein, R. 2018. Funding Long Shots, pre-print, MIT Laboratory for Financial Engineering.

R8: 4/25     *Securitization*  
*Immunology overview: T-cells, TCRs, and MHCs*

### L9: 4/30     Immunotherapeutics for Cancers

- A very gentle introduction to T cells and T cell receptors
- Activating natural anti-tumor T cells
- CAR-T cells

### Healthcare Analytics

- Estimation of clinical trial success rates in cancer
- Machine-learning applications to drug development

**Guest Speaker:** Michael Goldberg, Founder, StimIt

### Required Readings

- HFin: Chapter 10 (Healthcare Analytics)
- Wong, C., Siah, K. and Lo, A. 2018. Estimation of clinical trial success rates and related parameters in cancer. Preprint, MIT Laboratory for Financial Engineering.
- Yang, Y. Cancer immunotherapy: harnessing the immune system to battle cancer 2015 *J Clin Invest.* 125(9): 3335–3337.  
<https://www.ncbi.nlm.nih.gov/pubmed/26325031>

### Required Videos

- Immunology wars: Monoclonal antibodies
  - <https://www.youtube.com/watch?v=5AXApBbj1ps>
- Tumour immunology and immunotherapy
  - <https://www.youtube.com/watch?v=K09xzlQ8zsg>

### Assignments Due

- Pre-lecture readings quiz 9
- Problem set 8: Securitization

### Finance Advanced Readings

- Siah, K., Wong, C. and Lo, A. 2018. Machine-learning models for predicting drug approvals and clinical-phase transitions. Preprint, MIT Laboratory for Financial Engineering.
- Wong, C., Siah, K. and Lo, A. 2018. Estimation of clinical trial success rates and related parameters. *Biostatistics*  
<https://doi.org/10.1093/biostatistics/kxy072>.

### Biology Advanced Readings

- MCB pages 1104–1124: T cells and T cell receptors
- Jackson, H. et. al. 2016 Driving CAR T-cells forward *Nature Reviews Clinical Oncology* 13, pages 370–383  
<https://www.nature.com/articles/nrclinonc.2016.36>

### Optional Resources

- E. Dolgin. 2017. Epic \$12 billion deal and FDA’s approval raise CAR-T to new heights. *Nature Biotechnology*
- V. Prasad. 2017. Tisagenlecleucel — the first approved CAR-T cell therapy: implications for payers and policy makers. *Nature Rev. Clin. Oncology*
- Hay, M., Thomas, D. W., Craighead, J. L., Economides, C. and Rosenthal, J. 2014. Clinical development success rates for investigational drugs. *Nature Biotechnology*

R9: 5/2      *Healthcare Analytics*  
*Cancer immunotherapy*

## L10: 5/7 **Novel Cell Therapies**

- Embryonic Stem (ES) Cells and induced pluripotent stem (iPS) cells
- Diabetes: Production of insulin - producing islet cells
- Inherited metabolic and other disorders: Engineered red blood cells

### **Pricing, Insurance, and Ethics**

- Pharmaceutical pricing policies in the U.S. and abroad
- The economics and ethics of pricing and patient access

**Guest Speakers:** Rena Conti, Associate Professor, Boston University  
Bill Dreitlein, Senior Director, OptumRx (Formerly ICER)  
Jesper Høiland, CEO, Radius Health

### **Required Readings**

- HFin: Chapter 12 (Pricing, Value, and Ethics)
- Burnham, T., Huang, S., Lo, A. 2018. Pricing for survival in the biopharma industry: A case study of Acthar gel and Questcor Pharmaceuticals. *Journal of Investment Management*, 15, 69–91.
- Watson, S. and Freudenrich, C. How stem cells work: <https://science.howstuffworks.com/life/cellular-microscopic/stem-cell1.htm>

### **Assignments Due**

- Pre-lecture readings quiz 10
- Problem Set 9: Predictive analytics for drug approvals
- Final project due: Video presentation and slide deck

### **Finance Advanced Readings**

- ICER. 2018. *Chimeric Antigen Receptor T-Cell Therapy for B-Cell Cancers: Effectiveness and Value*. Boston, MA: ICER.

### **Biology Advanced Readings**

- MCB pages 980–986: ES and iPS cells
- Pagliuca, F. et al. (2014) Generation of functional human pancreatic  $\beta$  cells in vitro. *Cell* 159:428

### **Optional Resources**

- ICER. 2015. The Comparative Clinical Effectiveness and Value of Novel Combination Therapies for the Treatment of Patients with Genotype 1 Chronic Hepatitis C Infection: A Technology Assessment
- U.S. Government Accountability Office (GAO). 2009. *Brand-Name Prescription Drug Pricing*. Washington, DC: U.S. Government Publishing Office. <http://www.gao.gov/new.items/d10201.pdf>
- U.S. Government Accountability Office (GAO). 2016. *Generic Drugs Under Medicare*. Washington, DC: U.S. Government Publishing Office. <http://www.gao.gov/products/GAO-16-706>
- Senate Committee Print. 2015. *The Price of Sovaldi and its Impact on the U.S. Health Care System*, 114–20. Washington, DC: U.S. Government Publishing Office.

*R10: 5/9 No recitation for finance, but will be available for last minute consultation for projects  
Stem cell overview and therapeutic applications*

**L11: 5/14 Project Presentations**

- Student teams present their projects to the class and an external panel of judges: Amy Schulman, Anne Deconinck, Lita Nelsen, Krishna Yeshwant