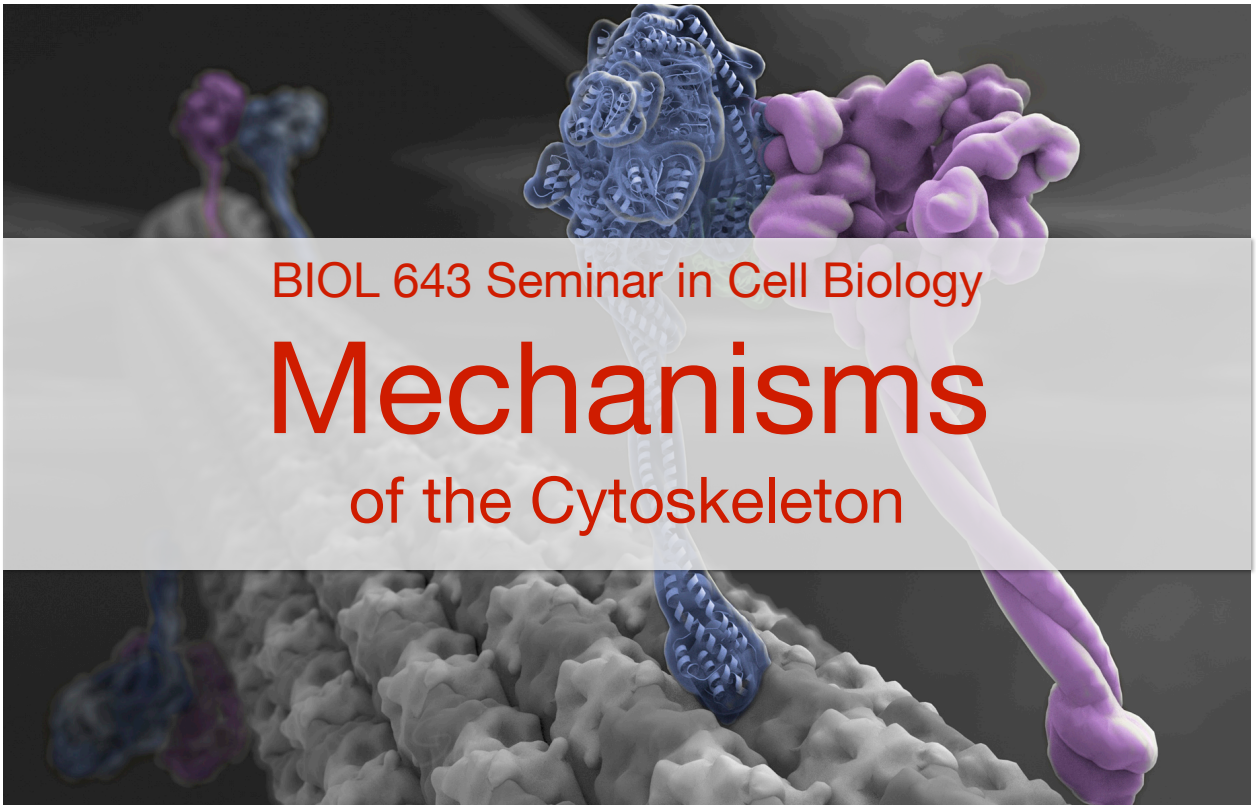

Meeting Time: Tuesdays & Thursdays, 2:00 pm – 3:15 pm (starting Tuesday, August 20th)

Meeting Location: Wilson Hall, Rm 310

Course Hours: 3

Instructors:

Kevin Slep	402 Fordham Hall	kslep@bio.unc.edu	919-962-4858
Steve Rogers	421 Fordham Hall	srogers@bio.unc.edu	919-843-7788

Overview:

This seminar focuses on molecular mechanisms of cytoskeletal components. The course will examine the actin cytoskeleton and the microtubule cytoskeleton. A sample of topics include 1) the core building blocks: actin and tubulin; 2) nucleators: Arp2/3 and gamma tubulin/gamma-TuRC/Augmin; 3) motors: myosin, kinesin and dynein; 4) regulators: formins and microtubule plus end binding proteins; 5) destabilizers: cofilin and stathmin; and 6) kinetochore-microtubule attachments complexes. Primary literature will be examined, presented and critiqued. Each topic will examine a molecular/mechanistic paper that correlates structure with mechanism. Emerging techniques in cell biology and structure will be discussed including single molecule fluorescent techniques (PALM, FIONA, speckle microscopy), and optical trapping. The seminar aims to develop presentation skills, scientific writing, as well as manuscript evaluation and critique.

Methodology:

As a seminar course, we will examine primary literature. Participation from all members is critical. Each week, papers will be presented to the group by one or two assigned members. During the presentation, the paper will be critiqued as a group. People presenting the paper will present the material via Powerpoint or

equivalent program. Additional papers assigned for the class will be examined in a round-table format. Be prepared to discuss the paper and the presenter should have familiarity with any supplemental material.

In order to familiarize students with the practice of reviewing papers for a journal, we will go over aspects of how to write a review of a manuscript for an editor. The student will choose one paper for review that focuses on a specific area of interest to them that overlaps with topics covered in class. The review will be due at assigned dates shown below.

In order to familiarize students with manuscript preparation techniques and the practice of reviewing papers for a journal, we will go over aspects of 1) writing cover letters to the editor for manuscript submission and 2) how to write a review of a manuscript for an editor. The student will prepare two cover letters, directed at the editor for two of the papers presented in the course. These mock cover letters will be presented to the class prior to going over the paper. The cover letters should be for papers for which the student is not leading the presentation. For the mock peer review paper assignments, students should choose a paper on a topic involving the cytoskeleton (search in PubMed) and check with the Instructors to make sure the article is appropriate for review. The two reviews will be due at assigned dates shown below.

At the final class (Saturday, Dec 7th), each student will give a mini-presentation on a recently published cytoskeletal paper that probes molecular/cellular mechanism. Papers should be selected by the student and approved by the instructors by Nov 21st. This manuscript should be distinct from the two manuscripts that the student based their two mock reviews on.

Grading:

Participation Throughout Course		30%
Presentations (3 x 15%)		45%
Cover Letters (2 x 2.5%)		5%
Reviews:	1st (Midterm)	7.5%
	2nd (Final Exam)	7.5
Final Mini Presentation		5%

Text:

No text required, this course examines primary literature that will be available on PubMed and available for download from the class Sakai site. Only the main body of the article will be posted on Sakai. Online access at the journal site will give you access to view movies and supplemental material related to the article. The easiest way to access this material is to search for the article on PubMed.

Exams:

The midterm exam and the final exam will take the form of the mock manuscript reviews outlined above. The midterm review will be due Tuesday, October 15th and the final exam review will be due on Saturday, December 7th.

Date	Topic	Paper Title
8/20/19	Course Overview	
Building Blocks		
8/22/19	Tubulin	McIntosh JR, O'Toole E, Morgan G, Austin J, Ulyanov E, Ataullakhanov R, Gudimchuk N. Microtubules grow by the addition of bent guanosine triphosphate tubulin to the tips of curved protofilaments. J Cell Biol. 2018 Aug 6;217(8):2691-2708.
8/27/19	Actin	Otterbein LR, Graceffa P, Dominguez R. The crystal structure of uncomplexed actin in the ADP state. Science. 2001 Jul 27;293(5530):708-11.
8/29/19	Bacterial actin	Garner EC, Campbell CS, Weibel DB, Mullins RD. Reconstitution of DNA segregation driven by assembly of a prokaryotic actin homolog. Science. 2007 Mar 2;315(5816):1270-4.
Nucleators at the minus end		
9/3/19	Patronin	Goodwin SS, Vale RD. Patronin regulates the microtubule network by protecting microtubule minus ends. Cell. 2010 Oct 15;143(2):263-74. doi: 10.1016/j.cell.2010.09.022.
9/5/19	Centrioles I	Kitagawa D, Vakonakis I, Olieric N, Hilbert M, Keller D, Olieric V, Bortfeld M, Erat MC, Flückiger I, GönczyP, Steinmetz MO.. Structural basis of the 9-fold symmetry of centrioles. Cell. 2011 Feb 4;144(3):364-75.
9/10/19	Centrioles II	Mennella V, Keszthelyi B, McDonald KL, Chhun B, Kan F, Rogers GC, Huang B, Agard DA. Subdiffraction-resolution fluorescence microscopy reveals a domain of the centrosome critical for pericentriolar material organization. Nat Cell Biol. 2012 Nov;14(11):1159-68. doi: 10.1038/ncb2597.
9/12/19	Arp2/3 I	Svitkina TM, Borisy GG. Arp2/3 complex and actin depolymerizing factor/cofilin in dendritic organization and treadmilling of actin filament array in lamellipodia. J Cell Biol. 1999 May 31;145(5):1009-26.
9/17/19	Arp2/3 II	Wu C, Asokan SB, Berginski ME, Haynes EM, Sharpless NE, Griffith JD, Gomez SM, Bear JE. Arp2/3 is critical for lamellipodia and response to extracellular matrix cues but is dispensable for chemotaxis. Cell. 2012 Mar 2;148(5):973-87. doi: 10.1016/j.cell.2011.12.034.

Tip Proteins

9/19/19	MT +Tips	Maurer SP, Fourniol FJ, Bohner G, Moores CA, Surrey T. EBs recognize a nucleotide-dependent structural cap at growing microtubule ends. Cell. 2012 Apr 13;149(2):371-82.
9/24/19	XMAP215	Brouhard GJ, Stear JH, Noetzel TL, Al-Bassam J, Kinoshita K, Harrison SC, Howard J, Hyman AA. XMAP215 is a processive microtubule polymerase. Cell. 2008 Jan 11;132(1):79-88. doi: 10.1016/j.cell.2007.11.043.
9/26/19	Formins	Otomo T, Tomchick DR, Otomo C, Panchal SC, Machius M, Rosen MK. Structural basis of actin filament nucleation and processive capping by a formin homology 2 domain. Nature. 2005 Feb 3;433(7025):488-94.
10/1/19	Kinetochores	Ciferri C, Pasqualato S, Screpanti E, Varetti G, Santaguida S, Dos Reis G, Maiolica A, Polka J, De Luca, JG, De Wulf P, Salek M, Rappsilber J, Moores CA, Salmon ED, Musacchio A. Implications for kinetochore-microtubule attachment from the structure of an engineered Ndc80 complex. Cell. 2008 May 2;133(3):427-39..

Post-translational Modifications

10/3/19	Post-translational Modifications	Szyk A, Deaconescu AM, Spector J, Goodman B, Valenstein ML, Ziolkowska NE, Kormendi V, Grigorieff N, Roll-Mecak A. Kormendi V, Grigorieff N, Roll-Mecak A. Molecular basis for age-dependent microtubule acetylation by tubulin acetyltransferase. Cell. 2014 Jun 5;157(6):1405-15.

Destabilizaers

10/8/19	Spastin & Katanin I	Roll-Mecak A, Vale RD. Structural basis of microtubule severing by the hereditary spastic paraplegia protein spastin. Nature. 2008 Jan 17;451(7176):363-7.
10/10/19	Spastin & Katanin II	Lindeboom JJ, Nakamura M, Hibbel A, Shundyak K, Gutierrez R, Ketelaar T, Emons AM, Mulder BM, Kirik V, Ehrhardt DW. A mechanism for reorientation of cortical microtubule arrays driven by microtubule severing. Science. 2013 Dec 6;342(6163):1245533. doi: 10.1126/science.1245533. Epub 2013 Nov 7.

10/15/19	Stathmin	Gigant B, Curmi PA, Martin-Barbey C, Charbaut E, Lachkar S, Lebeau L, Siavoshian S, Sobel A, Knossow M. The 4 A X-ray structure of a tubulin:stathmin-like domain complex. Cell. 2000 Sep 15;102(6):809-16. Ravelli RB, Gigant B, Curmi PA, Jourdain I, Lachkar S, Sobel A, Knossow M. Insight into tubulin regulation from a complex with colchicine and a stathmin-like domain. Nature. 2004 Mar 11;428(6979):198-202.
		MIDTERM REVIEW ASSIGNMENT DUE
10/17/19		**FALL BREAK - NO CLASS**
10/22/19	Cofilin I	Paavilainen VO, Oksanen E, Goldman A, Lappalainen P. Structure of the actin-depolymerizing factor homology domain in complex with actin. J Cell Biol. 2008 Jul 14;182(1):51-9. Jansen S, Collins A, Chin SM, Ydenberg CA, Gelles J, Goode BL. Single-molecule imaging of a three-component ordered actin disassembly mechanism. Nat Commun. 2015 May 21;6:7202.
10/24/19	Cofilin II	Johnston AB, Collins A, Goode BL. High-speed depolymerization at actin filament ends jointly catalysed by Twinfilin and Srv2/CAP. Nat Cell Biol. 2015 Nov;17(11):1504-11. doi: 10.1038/ncb3252. Epub 2015 Oct 12.
Cross-linkers		
10/29/19	Crosslinkers	Preciado López M, Huber F, Grigoriev I, Steinmetz MO, Akhmanova A, Koenderink GH, Dogterom M. Actin-microtubule coordination at growing microtubule ends. Nat Commun. 2014 Aug 27;5:4778. doi: 10.1038/ncomms5778.
Motors		
10/31/19	Kinesin I	Mori T, Vale RD, Tomishige M. How kinesin waits between steps. Nature. 2007 Nov 29;450(7170): 750-4. Epub 2007 Nov 14.
11/5/19	Kinesin II	Kaan HY, Hackney DD, Kozielski F. The structure of the kinesin-1 motor-tail complex reveals the mechanism of autoinhibition. Science. 2011 Aug 12;333(6044):883-5

11/7/19	Dynein I	Redwine WB, Hernández-López R, Zou S, Huang J, Reck-Peterson SL, Leschziner AE. Structural basis for microtubule binding and release by dynein. Science. 2012 Sep 21;337(6101):1532-6.
11/12/19	Dynein II	Toropova K, Zou S, Roberts AJ, Redwine WB, Goodman BS, Reck-Peterson SL, Leschziner AE. Lis1 regulates dynein by sterically blocking its mechanochemical cycle. Elife. 2014 Nov 7;3. doi: 10.7554/eLife.03372.
11/14/19	Dynein III	Urnavicius L, Zhang K, Diamant AG, Motz C, Schlager MA, Yu M, Patel NA, Robinson CV, Carter AP. The structure of the dynactin complex and its interaction with dynein. Science. 2015 Mar 27;347(6229):1441-6.
11/19/19	Myosin I	Ménétrey J, Llinas P, Mukherjea M, Sweeney HL, Houdusse A. The structural basis for the large powerstroke of myosin VI. Cell. 2007 Oct 19;131(2): 300-8.
11/21/19	Myosin II	Kodera N, Yamamoto D, Ishikawa R, Ando T. Video imaging of walking myosin V by high-speed atomic force microscopy. Nature. 2010 Nov 4;468(7320):72-6.
11/26/19	Motor Wars I	Derr ND, Goodman BS, Jungmann R, Leschziner AE, Shih WM, Reck-Peterson SL. Tug-of-war in motor protein ensembles revealed with a programmable DNA origami scaffold. Science. 2012 Nov 2;338(6107):662-5. doi: 10.1126/science.1226734. Epub 2012 Oct 11.
11/28/19		**THANKSGIVING RECESS - NO CLASSES**
12/3/19	Motor Wars II	Stepanek L, Pigino G. Microtubule doublets are double-track railways for intraflagellar transport trains. Science. 2016 May 6;352(6286):721-4. doi: 10.1126/science.aaf4594. Epub 2016 May 5 Nakamura M, Chen L, Howes SC, Schindler T, Nogales E, Bryant Z. Remote control of myosin and kinesin motors using light-activated gearshifting. Nat Nanotechnol. 2014 Aug 3. doi: 10.1038/nnano.2014.147.
12/7/19		**SPECIAL TOPICS PRESENTATIONS** **FINAL REVIEW ASSIGNMENT DUE**