Publications:

- Signal Transduction During Development in Dictyostelium Discoideum

The ability of mammalian cells to sense the density of the cells around them play an important role in cellular growth control and differentiation. Without such an ability, a developing embryo would be unable to properly proportion its cells into different tissue types. Unfortunately, studying this phenomenon in mammals is made difficult due to their complexity and genetic intractability. Therefore, we study cell-density, or quorum sensing in the simple eukaryote Dictyostelium discoideum.

Dictyostelium normally exist as vegetative amoebae that feed on bacteria and multiply by fission. When the amoebae overgrow their food source, they aggregate using relayed pulses of cAMP as a chemoattractant. The aggregate then elongates forming a mobile slug, which migrates and eventually forms a fruiting body consisting of a mass of spore cells situated on top of a column of stalk cells. The entire process takes 24 hours, but will not begin unless the density of starving cells is high enough to allow formation of an sized fruiting body. The starving cells are able to sense the density of the cells around them by simultaneously secreting and sensing a protein called CMF. Only when the cells are at a high density, as determined by high levels of CMF, will the cells initiate development. We study the signal transduction pathways activated by CMF and how they impact upon other developmental pathways. We have found that CMF regulates development by modulating the cell's ability to respond to cAMP. Specifically, it regulates the G protein associated with the cAMP receptor. We are currently examining the roles of phospholipase D, cell adhesion and GTPase activating proteins in this process.

Selected Publications:

- Santiago, Z., Loustau, J., Meretzky, D., Rawal, D., Brazill, D. (2019) <u> Advances in geometric techniques for analyzing blebbing in chemotaxing Dictyostelium cells.</u>
 PLOS ONE 14(2): e0211975.
- Mohamed, W., Ray, S., Brazill, D., Ramamurthy, B. (2015). Absence of catalytic domain in a putative protein kinase C (PkcA) suppresses tip dominance in Dictyostelium discoideum. Dev Biol. 405(1): 10-20
- Garcia M, Ray S, Brown I, Irom J, Brazill D. (2014). PakD, a Putative p21-Activated Protein Kinase in Dictyostelium discoideum, Regulates Actin. Euk Cell. 13(1):119-26
- Garcia, R., Nguyen, L., and Brazill, D. (2013). Dictyostelium discoideum SecG interprets cAMP mediated chemotactic signals to influence actin organization. Cytoskeleton. 70(5):269-80

- Maharjan, A., Roife, D., Brazill, D., and Gomer, R. (2013). Serum amyloid P inhibits granulocyte adhesion. Fibrogenesis and Tissue Repair. 6(1):2-18
- Pribic, J., and Brazill, D. (2012). Paxillin phosphorylation and complexing with Erk and FAK are regulated by PLD activity in MDA-MB-231 cells. Cell Signal. 24: 1531-1540
- Pribic, J., Garcia, R., Kong, M. and Brazill, D. (2011). Paxillin and Phospholipase D interact to regulate actin-based process in Dictyostelium discoideum. Euk. Cell. 10(7):977-84
- Gomer, R., Jang, W., Brazill, D. (2011). Cell Density Sensing and Size Determination. Dev. Growth. Diff. 53(4):482-94.
- Ray, S., Chen, Y., Ayoung, J., Hanna, R. and Brazill, D. (2011). Phospholipase D Controls Dictyostelium Development By Regulating G Protein Signaling. Cell Signal 23(2):335-43.
- Duran, M.B., Rahman, A., Colten, M., Brazill, D. (2009) Dictyostelium discoideum Paxillin Regulates Actin-Based Processes. Protist 160(2):221-32
- Deenadayalan, B., Brazill, D. Gomer, R., H., Eichinger, L., Rivero, F., Noegel, A., A. (2007) An unusual G protein coupled receptor mediates cell density sensing in Dictyostelium. Current Biology, 17(10):
- Brazill, D. and Gomer, R.H. (2008) Brazill, "A eukaryotic neighbor: Dictyostelium discoideum." Myxobacteria: Multicellularity and Differentiation (2008): 439-452.
- Thomason, P., A., Brazill, D., T and Cox, E., C.(2006) A Series of Dictyostelium Expression Vectors for Use With Recombination Cloning. Plasmid 56(3): 142 152
- Chen. Y.., Rodrick, V., Yan, Y., Brazill, D. (2005) PldB, a Phospholipase D Homologue in Dictyostelium discoideum mediates quorum sensing during development. Euk Cell. 4: 694-702.
- Gomer, R.H. and Brazill, D.T. (2003) The versatile Dictyostelium discoideum. Meeting Report: International Dictyostelium Conference 2002. Protist 154, 11-16.
- Bishop, J.D., Moon, B.C., Ratner, D., Dottin, R.P., Gomer, R.H., Brazill, D.T. (2002) A second UDP-glucose pyrophosphorylase is required for differentiation and development in Dictyostelium discoideum. J Biol Chem 277:32430-32437.
- Azhar, M., Kennady, PK., Pande, G., Espiritu, M., Holloman, W., Brazill, D., Gomer, RH., Nanjundiah, V. Cell cycle phase, cellular Ca2+ and development in Dictyostelium discoideum. Int J Dev Biol. 2001 Apr;45(2):405-14.
- Brazill, D.T., Meyer, L.R., Diane Hatton, Debra A. Brock, Gomer, R.H. (2001) ABC transporters required for endocytosis and endosomal pH regulation in Dictyostelium J Cell Sci. 2001 Nov 1;114(Pt 21):3923-3932.
- Brazill, D.T., Lindsey, D.F., Bishop, J.D., and Gomer, R.H. (1998) Cell-density sensing mediated by a G-protein-coupled receptor activating phospholipase C. J Biol Chem. 273, 8161-8168.
- Brazill, D.T., Gundersen, R. and Gomer, R.H. (1997) A cell-density sensing factor regulates the lifetime of a chemoattractant-induced Ga-GTP conformation. FEBS Letters 404, 100-104.
- Jain, R., Brazill, D.T., Cardelli, J.T., Bush, J., and Gomer, R.H. (1997) Autocrine factors controlling early development. In Dictyostelium-A Model System for Cell and

Developmental Biology. (Y. Maeda, K. Inouye, and I. Takeuchi, Eds.) Universal Academy Press, Inc., Tokyo, Japan. pp. 219-234.

- Chen. Y.., Rodrick, V., Yan, Y., Brazill, D. (2005) PldB, a Phospholipase D Homologue in Dictyostelium discoideum mediates quorum sensing during development.