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Motor force regulation in skeletal muscle contraction

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Objective In skeletal muscle contraction, individual myosin motors appear to randomly attach to and detach from actin filaments, while multiple motors can perform coordinated and synchronous actions. How order out of chaos in this system is an intriguing issue. **Methods** With a multiple scale model for skeletal muscle contraction, we theoretically investigate this issue with coupled Finite Element method and Monte Carlo simulation method. **Results** We show that the unique force-stretch relation of myosin motor is critical to cause the average number of working motors to increase in linear proportion to the filament load so that the motor force is rather precisely regulated. We also show that the stochastic features of an ATP hydrolysis cycle can be sufficient while those of catch-slip bonds can be dispensable for motor force regulation. At the level of a single motor, we hypothesize that a "working" motor is arrested in a transitional state when the motor force is ~6 pN, based on which the unique force-stretch relation of myosin motor is recovered. We also investigate the temperature effect on various aspects of the power stroke of a working motor. Our analysis suggests that, though swing rates, the isometric force, and the maximal stroke size all strongly vary with the temperature, the temperature can have a very small effect on the releasable elastic energy within the power stroke. **Conclusions** Our theoretical studies are consistent with many experimental results and provide important insights into understanding motor force regulation in skeletal muscle contraction. (NSFC:11572285,11621062)

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基底力学微环境调控胚胎干细胞肝向分化的规律及分子机制

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目的 通过建立硬度耦合拓扑结构基底影响胚胎干细胞(embryonic stem cell, ESCs)肝向分化的实验体系,深化力学微环境对ESCs肝向分化的生物学过程及力学-生物学耦合规律及分子机制的认识,为阐明力致ESCs肝向分化的生理及体外调控过程提供基础数据,并为肝脏疾病治疗和工程化肝组织构建研究提供新思路、新视角。**方法** 将聚丙烯酰胺水凝胶按特定配比制备不同硬度、拓扑结构及两者耦合的基底力学微环境,建立不同硬度耦合拓扑结构基底ESCs黏附生长及肝向分化的实验体系。采用实时定量PCR、免疫荧光、流式细胞术、蛋白质免疫印迹、糖原染色、ICG吞噬及药物代谢等技术方法,研究不同力学微环境诱导分化得到的类肝细胞的功能和成熟度,同时对分化不同阶段细胞的力学性质进行检测。**结果** 硬度和拓扑在ESCs肝向分化的不同阶段作用不同:硬胶主要调控分化前期,软胶在分化后期作用明显;拓扑结构随分化作用逐渐减弱;拓扑和硬度两者耦合可明显影响分化进程和成熟度,特定的硬度和拓扑有利于ESCs分化成肝细胞。此外,分化得到的肝细胞与生理肝细胞力学性质相当,硬度较拓扑可更明显影响细胞的力学性质。**结论** ESCs肝向分化及体外肝细胞培养中基底硬度和拓扑具有协同效应,可提高分化所得肝细胞效率、成熟度和功能。 (国家自然科学基金资助项目,Nos. 31230027, 31661143044, 31627804)