

Status of Satellite Cell Research in Agriculture

Michael Dodson, Douglas McFarland⁽¹⁾, Everett Bandman⁽²⁾, William Dayton⁽³⁾, Zipora Yablonka-Reuveni⁽⁴⁾, Elizabeth Greene, Matthew Doumit⁽⁵⁾, Werner Bergen⁽⁵⁾, Robert Merkel⁽⁵⁾, Janet Vierck, Sandra Velleman⁽⁶⁾ and Joseph Koumans⁽⁷⁾

Muscle Biology Laboratory, Department of Animal Sciences, Washington State University, Pullman, USA; (1) Muscle Biology Laboratory, Department of Animal and Range Sciences, South Dakota State University, Brookings, USA; (2) Department of Food Science and Technology, University of California at Davis, Davis, USA; (3) Andrew Boss Laboratory, Department of Animal Sciences, University of Minnesota, St Paul, USA; (4) Department of Biological Structure, University of Washington, Seattle, USA; (5) Growth Biology Program, Department of Animal Science, Michigan State University, East Lansing, USA; (6) Departments of Animal Sciences and Animal Genetics, University of Connecticut, Storrs, USA and (7) Laboratoire D'Anatomie Comparée, Université Paris 7, France.

Key words: skeletal muscle, satellite cell, domestic animals, poultry, fish.

BAM 5 (1): 5-9, 1995

For centuries, meat-producing animals have been phenotypically selected for efficiency of feed conversion, variables of carcass quality and yield of total carcass lean (meat). Research in animal nutrition and animal genetics flourished and, until recently, provided the core of knowledge presently available concerning muscle growth dynamics in meat-producing animals. Today, research in allied animal science disciplines such as muscle biology or animal growth biology are providing additional details of cellular muscle growth mechanisms, including participation of myogenic satellite cells [38] in facilitating postnatal muscle growth.

The major postnatal muscle growth component for traditional meat animals is hypertrophy [50], but in fish myofiber hyperplasia may occur as a normal mechanism of growth until late in adulthood [24, 33, 34, 53, 55]. Satellite cells appear to be important during both myofiber hyperplasia and hypertrophy. They enhance the myonuclei population and thereby facilitate protein accretion in normal myofibers during hypertrophy [47, 48] and appear to be responsible for myofiber hyperplasia and regeneration [3, 4, 8, 34, 36, 38].

Studies with satellite cells from laboratory species [3, 25, 59] have translated to successful experiments with domestic animal-derived satellite cells [Table 1]. Meat animal-derived satellite cells possess characteristics similar to satellite cells from laboratory species. The *in vivo* locale, positioned adjacent to myofibers and wedged between the

sarcolemma and basement membrane, the high nuclear: cytoplasmic ratio, type and amount of cytoplasmic organelles, and distribution of cells in muscle as a function of age appear to be homologous across species [1, 8, 38].

Methods used to isolate domestic animal-derived satellite cells for subsequent study in cell culture were adapted from techniques originally established for isolation of rat satellite cells [2, 6, 13, 14, 15, 22, 31, 40, 59]. Most domestic animal satellite cells require a protein substratum for attachment to cell cultureware [12, 14, 15, 22, 40]. Following attachment, satellite cells appear to be capable of proliferation in response to increasing levels of serum contained within traditional growth media [39]. Further, differentiation of satellite cells seems to be triggered by serum reduction methods [2, 3, 14, 15, 39]. Other *in vitro* characteristics include the capability of satellite cells to remain viable in serum-free defined medium [3, 11, 43], and comparable responses of cells to individual growth factors contained within the defined medium [4, 10, 17, 21, 39, 43].

Although many similarities exist between satellite cells from all animals, it is difficult to extrapolate satellite cell culture data from system to system. Species differences account for some of the variability observed between systems. For example, chicken-derived satellite cells require chicken embryo extract for growth to occur in culture [26, 27, 29, 59]; chicken satellite cells lack a type II IGF receptor [18, 20], and beef cattle-derived satellite cells

Satellite cell research

Table 1: Summary of agriculturally-important animal satellite cell research with references associated to different scientific emphasis areas.

RESEARCH AREA	REFERENCE
A. <i>In vivo</i> :	
(morphology/comparative/physiology)	7,8,9,32,37
B. <i>In vitro</i> :	
1. Cell culture system development	
-sheep	11,12,13,30,35,45,46,52
-beef	5,14,21
-turkey	16,40,41,42,43,44,54
-chicken	18,19,26,27,28,29,36,59
-horse	22
-pig	10,15,17
-fish	23,31,51
2. Myogenesis studies	
-cell cycle regulation (activation/proliferation/differentiation)	2,10,11,12,17,20,21,28,30,33, 40,41,42,43,58,59
-Myotube maturation (protein profile regulation)	5,26,27,36,45,46
3. Metabolism studies	18,19,52
4. Myogenic cell comparison	
-embryonic myoblasts to satellite cells	26,29,42,49,54,57
-satellite cells to satellite cells	27,33,45,46
-satellite cells from different animals	5,11,16,35,41
C. Review Papers	3,4,8,39,56

respond inconsistently to TGF- β and other growth factors [21]. Data also suggest that meat-type animals such as chickens [27], sheep [45, 46] and fish [33, 34] possess different subclasses of satellite cells, which may be activated by different muscle growth requirements [33, 34]. These examples illustrate that meat animal-derived satellite cells display distinct physiological properties, that if further exploited, may aid in defining novel aspects of postnatal myogenesis.

Currently, research with meat animal-derived satellite cell systems is focused on three priority areas. The first priority area is definition of the mechanisms involved in activating satellite cells from a dormant to a proliferating condition. Research in this area includes devising more efficient and repeatable methods to isolate satellite cells from a variety of individual muscles, determining optimal conditions for isolated satellite cells to attach and survive *in vitro*, elucidation of the presence of satellite cells that are derived from different lineages that might possess different biochemical and biophysical properties, and definition of activating factors that promote satellite cell transit through the cell cycle. The second priority area is definition of regulatory factors that influence satellite cell proliferation and differentiation in cell culture. Factors that have been identified to exert muscle growth effects *in vivo*

have been screened for effects on satellite cells *in vitro* and mechanisms of action are now being defined. Most of the resources available for domestic animal satellite cell research are derived from agencies interested in future exploitation of data derived from this research area. The third priority involves the study of the regulation that satellite cell-derived myonuclei exerts on myofibers, during events facilitating myofiber hypertrophy. For researchers studying domestic animal-derived satellite cells, application of long-term research endpoints are likely to 1) provide practical ways to enhance the efficiency of lean muscle growth and thereby reduce feeding of energy and protein sources to meat animals; 2) enhance the body composition of meat animals to improve the yield of edible product; 3) improve meat quality; 4) provide alternative method(s) or criteria for genetic selection of replacement animals; 5) serve as important comparison systems to identify mechanisms for muscle response to exercise; and 6) serve as models for human myopathy research.

In summary, a complete understanding of mechanisms involved in postnatal skeletal muscle growth in domestic animals requires knowledge of how myogenic satellite cells participate in the growth process. As domestic animal-derived satellite cell culture systems become available, their utility in addressing variables of satellite cell

involvement in postnatal muscle growth mechanisms will be recognized. This compilation of research articles is an attempt to examine characteristics of myogenic satellite cells from several meat-producing domestic animals, including data from avian, horse and fish species as these animals provide considerable amounts of edible protein, worldwide. Contributors of this *BAM* volume appreciate the opportunity to share basic and applied data, collected from use of animal-derived satellite cell systems.

Acknowledgments

The assistance of Ms. L.L. Clark and Ms. J. Hume in manuscript preparation is appreciated. Washington State Agricultural Research Center paper number 8095.

Address correspondence to:

M.V. Dodson, Ph.D., 207 Clark Hall, Muscle Biology Laboratory, Department of Animal Sciences, Washington State University, Pullman, WA 99164-6320, tel. (509) 335-9644, fax (509) 335-1082.

References

- [1] Allen RE, Merkel RA, Young RB: Cellular aspects of muscle growth: Myogenic cell proliferation. *J Animal Sci* 1979; 49: 115-127.
- [2] Allen RE, Dodson MV, Luiten LS: Regulation of skeletal muscle satellite cell proliferation by bovine pituitary fibroblast growth factor. *Exp Cell Res* 1984; 152: 154-160.
- [3] Allen RE: Muscle cell culture as a tool in animal growth research. *Fed Proc* 1987; 46: 290-294.
- [4] Allen RE, Rankin LL: Regulation of satellite cells during skeletal muscle growth and development. *Proc. Soc. Exp. Biol. & Med.* 1990; 194: 81-86.
- [5] Allen RE, Rankin LL, Greene EA, Boxhorn LK, Johnson SE, Taylor RG, Pierce PR: Desmin is present in proliferating rat muscle satellite cells but not in bovine muscle satellite cells. *J Cellular Physiol* 1991; 149: 525-535.
- [6] Bischoff R: Enzymatic liberation of myogenic cells from adult rat muscle. *Anat Rec* 1974; 180: 645-652.
- [7] Champion DR, Richardson RL, Reagan JO, Kraeling RR: Changes in the satellite cell population during postnatal growth of pig skeletal muscle. *J Animal Sci* 1983; 52: 1014-1018.
- [8] Champion DR: The muscle satellite cell: A review. *Int Rev Cytology* 1984; 87: 225-251.
- [9] Champion DR, Seerley RW, Kveragas CL: Effect of maternal dietary fat on skeletal muscle cellularity and satellite cell content of the porcine fetus at 110 days of gestation. *Acta Anat* 1984; 120: 170-172.
- [10] Cook DR, Doumit ME, Merkel RA: Transforming growth factor-beta, basic fibroblast growth factor, and platelet-derived growth factor-BB interact to affect proliferation of clonally derived porcine satellite cells. *J Cellular Physiol* 1993; 157: 307-312.
- [11] Dodson MV, Mathison BA: Comparison of ovine and rat muscle-derived satellite cells: Response to insulin. *Tissue and Cell* 1988; 20: 909-918.
- [12] Dodson MV, Mathison BA, Mathison BD: Effects of medium and substratum on ovine satellite cell attachment, proliferation and differentiation in vitro. *Cell Differentiation and Development* 1990; 29: 59-66.
- [13] Dodson MV, McFarland DC, Martin EL, Brannon MA: Isolation of satellite cells from ovine skeletal muscle. *J Tiss Culture Meth* 1986; 10: 233-237.
- [14] Dodson MV, Martin EL, Brannon MA, Mathison BA, McFarland DC: Optimization of bovine satellite cell-derived myotube formation in vitro. *Tissue and Cell* 1987; 19: 159-166.
- [15] Doumit ME, Merkel RA: Conditions for isolation and culture of porcine myogenic satellite cells. *Tissue and Cell* 1992; 24: 253-262.
- [16] Doumit ME, McFarland DC, Minshall RD: Satellite cells of growing turkeys: Influence of donor age and sex on proliferation and differentiation in vitro. *Exp Cell Res* 1990; 189: 81-86.
- [17] Doumit ME, Cook DR, Merkel RA: Fibroblast growth factor, insulin-like growth factors, and platelet-derived growth factor-BB stimulate proliferation of clonally derived porcine myogenic satellite cells. *J Cellular Physiol* 1993; 157: 326-332.
- [18] Duclos MJ, Chevalier B, Goddard C, Simon J: Regulation of amino acid transport and protein metabolism in myotubes derived from chicken muscle satellite cells by insulin-like growth factor-I. *J Cellular Physiol* 1993; 157: 650-657.
- [19] Duclos MJ, Chevalier B, Le Marchand-Brustel Y, Tanti JF, Goddard C, Simon J: Insulin-like growth factor-I stimulated glucose transport in myotubes derived from chicken muscle satellite cells. *J Endocrinol* 1993; 137: 465-472.
- [20] Duclos MJ, Wilkie RS, Goddard C: Stimulation of DNA synthesis in chicken muscle satellite cells by insulin and insulin-like growth factors: Evidence for exclusive mediation by a type-I insulin-like growth factor receptor. *J Endocrinol* 1991; 128: 35-42.

- [21] Greene EA, Allen RE: Growth factor regulation of bovine satellite cell growth *in vitro*. *J Animal Sci* 1991; 69: 146-152.
- [22] Greene EA, Raub RH: Procedures for harvesting satellite cells from equine skeletal muscle. *J Equine Vet Sci* 1992; 12: 33-35.
- [23] Greenlee AR, Dodson MV, Yablonka-Reuveni Z, Kersten CA, Cloud JG: *In vitro* differentiation of myoblasts from skeletal muscle of rainbow trout *Oncorhynchus mykiss*. *J Fish Biol* 1994 in press.
- [24] Greer-Walker M: Growth and development of the skeletal muscle fibers of the cod (*Gadus morhua*). *J Cons Int Explor Mer* 1970; 33: 228-244.
- [25] Grounds MD, Yablonka-Reuveni Z: Molecular and cell biology of muscle regeneration. In: *Molecular and Cell Biology of Muscular Dystrophy* (T. Partridge Ed) Chapman and Hall, London 1993; 210-256.
- [26] Feldman JL, Stockdale FE: Temporal appearance of satellite cells during myogenesis. *Dev Biol* 1992; 153: 217-226.
- [27] Feldman JL, Stockdale FE: Skeletal muscle satellite cell diversity: Satellite cells form fibers of different types in cell culture. *Dev Biol* 1991; 143: 320-334.
- [28] Halevy O, Lerman O: Retinoic acid induces adult muscle cell differentiation mediated by the retinoic acid receptor- α . *J Cellular Physiol* 1993; 154: 566-572.
- [29] Hartley RS, Bandman E, Yablonka-Reuveni Z: Skeletal muscle satellite cells appear during late chicken embryogenesis. *Dev Biol* 1992; 153: 206-216.
- [30] Hathaway MR, Hembree JR, Pampusch MS, Dayton WR: Effect of transforming growth factor β -1 on ovine satellite cell proliferation and fusion. *J Cellular Physiol* 1991; 146: 435-441.
- [31] Koumans JTM, Akster HA, Dulos GJ, Osse JWM: Myosatellite cells of *Cyprinus carpio* (Teleostei) *in vitro*: isolation, recognition and differentiation. *Cell Tissue Research* 1990; 261: 173-181.
- [32] Koumans JTM, Akster HA, Booms GHR, Lemmons CJJ, Osse JWM: Numbers of myosatellite cells in white axial muscle of growing fish: *Cyprinus carpio* (Teleostei). *Am J Anat* 1991; 192: 418-425.
- [33] Koumans JTM, Akster HA, Booms GHR, Osse JWM: Influence of fish size on proliferation and differentiation of cultured myosatellite cells of white axial muscle of carp. *Differentiation* 1993a; 53: 1-6.
- [34] Koumans JTM, Akster HA, Booms GHR, Osse JWM: Growth of carp (*Cyprinus carpio*) white axial muscle; the occurrence of hyperplasia and hypertrophy in relation to trunk weight, the myonucleus/sarcoplasm ratio and the occurrence of different subclasses of myogenic cells. *J Fish Biol* 1993b; 43: 69-80.
- [35] Mathison BD, Mathison BA, McNamara JP, Dodson MV: Insulin-like growth factor I receptor analyses of satellite cell-derived myotube membranes established from two lines of targhee rams selected for growth rate. *Dom Animal Endocrinol* 1989; 6: 191-201.
- [36] Matsuda R, Spector DH, Strohman RC: Regenerating adult chicken muscle and satellite cell cultures express embryonic patterns of myosin and tropomyosin isoforms. *Dev Biol* 1983; 100: 478-488.
- [37] Matthew CA, Moore MJ: Numbers of myonuclei and satellite cell nuclei in latissimus dorsi muscles of the chicken. *Cell Tissue Res* 1987; 248: 235-238.
- [38] Mauro A: Satellite cell of skeletal muscle fibers. *Biophys Bioch Cytol* 1961; 9: 493-495.
- [39] McFarland DC: Cell culture as a tool for the study of poultry skeletal muscle development. *J Nutrition* 1992; 122: 818-829.
- [40] McFarland DC, Doumit ME, Minshall RD: The turkey myogenic satellite cell: Optimization of *in vitro* proliferation and differentiation. *Tissue & Cell* 20: 1988; 899-908.
- [41] McFarland DC, Pesall JE, Gilkerson KK, Swenning TA: Comparison of the proliferation and differentiation of myogenic satellite cells derived from Merriam's and commercial varieties of turkeys. *Com Bioch Phys* 1993; 104: 455-460.
- [42] McFarland DC, Pesall JE, Gilkerson KK: The influence of growth factors on turkey embryonic myoblasts and satellite cells *in vitro*. *Gen Com Endocrinol* 1993; 89: 415-424.
- [43] McFarland DC, Pesall JE, Norberg JM, Dvoracek MA: Proliferation of the turkey myogenic satellite cell in a serum-free medium. *Com Bioch Biophys* 1991; 99A: 163-167.
- [44] Minshall RD, McFarland DC, Doumit ME: Interaction of insulin-like growth factor I with turkey satellite cells and satellite cell-derived myotubes. *Dom Animal Endocrinol* 1990; 7: 413-424.
- [45] Molnar G, Dodson MV: Characterization of sheep semimembranosus muscle and associated satellite cells: Expression of fast and slow myosin heavy chain. *Basic Applied Myology* 1992; 2: 183-190.

Satellite cell research

- [46] Molnar G, Dodson MV: Satellite cells isolated from sheep skeletal muscle are not homogeneous. *Basic Applied Myology* 1993; 3: 173-180.
- [47] Moss FP, LeBlond CP: Nature of dividing nuclei in skeletal muscle of growing rats. *J Cell Biol* 1970; 44: 459-462.
- [48] Moss FP, LeBlond CP: Satellite cells as the source of nuclei in muscles of growing rats. *Anat Rec* 1971; 170: 421-436.
- [49] Nameroff M, Rhodes LD: Differential response among cells in the chick embryo myogenic lineage to photosensitization by merocyanine 540. *J Cellular Physiol* 1989; 141: 475-482.
- [50] Pearson AM, Young RB: Skeletal muscle growth and protein metabolism, in Pearson AM, Young RB (eds): *Muscle and Meat Biochemistry*. New York, Acad Press, Inc., 1989, pp 216-234.
- [51] Powell RL, Dodson MV, Cloud JG: Cultivation and differentiation of satellite cells from skeletal muscle of the rainbow trout *Salmo gairdneri*. *J Exp Zool* 1989; 250: 333-338.
- [52] Roe JA, Harper JMM, Buttery PJ: Protein metabolism in ovine primary muscle cultures derived from satellite cells: Effects of selected peptide hormones and growth factors. *J Endocrinol* 1989; 122: 565-571.
- [53] Strickland AH, Gill HS: Growth and development of muscle fibers in the rainbow trout (*Salmo gairdneri*). *J Anat* 1983; 137: 323-333.
- [54] Sun SS, McFarland DC, Ferrin NH, Gilkerson KK: Comparison of insulin-like growth factor interaction with satellite cells and embryonic myoblasts derived from the turkey. *Comp Biochem Physiol* 1992; 102A: 235-243.
- [55] Weatherly AH, Gill HS: Growth dynamics of white myotomal muscle fibers in the bluntnose minnow *Pimephales notatus rafinesque* and comparison with rainbow trout *Salmo gairdneri richardson*. *J Fish Biol* 1984; 25: 13-24.
- [56] Yablonka-Reuveni Z: Development and postnatal regulation of adult myoblasts. *Microscopy Research and Techniques* 1994; in press.
- [57] Yablonka-Reuveni Z, Nameroff M: Temporal differences in desmin expression between myoblasts from embryonic and adult chicken skeletal muscle. *Differentiation* 1990; 45: 21-28.
- [58] Yablonka-Reuveni Z, Seifert RA: Proliferation of chicken myoblasts is regulated by specific isoforms of platelet-derived growth factor: Evidence for differences between myoblasts from mid and late stages of embryogenesis. *Dev Biol* 1993; 156: 307-318.
- [59] Yablonka-Reuveni Z, Quinn LS, Nameroff M: Isolation and clonal analysis of satellite cells from chicken pectoralis muscle. *Dev Biol* 1987; 119: 252-259.