OSU RESEARCH IN MUSCLE BIOLOGY

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In the first year we have completed several studies. Results of these studies are summarized briefly below.

FASTING STUDY (M.A. lian, GRA). Mechanisms by which muscle proteins are degraded in normal animals are not well understood. To gain insight into these processes, we use models in which muscle protein degradation is altered from its normal state, and characterize the changes which occur within the model. Fasting provides a convenient means by which we may study muscle protein degradation under stimulated conditions.

Fasting increases muscle protein degradation and causes a small increase in activities of proteolytic enzymes. When we assayed mechanisms accounting for changes in enzyme activities, we determined that messenger RNA (mRNA) concentrations encoding proteolytic enzymes were increased in skeletal muscle and were either unaffected or reduced in other tissues. Hence, the regulation of muscle proteinase gene expression appears to differ from regulation in other tissues. We plan to follow up on these observations by trying to identify the agent in blood which mediates changes in mRNA levels arise from changes in rates of transcription of the genes encoding the proteinases. This work has been supported by a USDA grant awarded to N. Forsberg in 1988.

EFFECTS OF CASTRATION ON GROWTH (B.R. Ou, GRA). In a study with sheep we undertook a project to investigate how castration affects muscle growth. Castration did not affect lamb growth until after weaning. After weaning, ram growth rate to market weight exceeded that of wethers by 17 percent. Muscle weights of rams at market weight were also larger than muscle weights of wethers. To determine whether the larger rates of muscle growth of intact rams were due to lower rates of protein degradation, we assayed activities of proteolytic enzymes in ram and wether muscle samples and found no differences. Hence, we conclude that castration effects a reduction in muscle growth by reducing muscle protein synthesis.

EFFECTS OF AGING ON MUSCLE GROWTH (B.R. Ou, GRA). As animals age, rates of muscle growth are reduced. This is associated with reductions in rates of both muscle protein synthesis and muscle protein degradation. The mechanisms underlying age-dependent attenuation of muscle protein degradation have not been identified. In two studies (one with lambs and one with rabbits) we investigated this process. We found that age-dependent attenuation of protein degradation is caused by 3 processes:

a. as animals age, proteins accumulate in muscles and these proteins dilute the specific activities of muscle proteinases,

b. protein synthetic capacity (RNA content) of muscle declines as animals age. Hence, fewer proteinases will be synthesized in older animals, and

c. Messenger RNA concentrations encoding proteinases decline as animals age. This is not the result of specific down-regulation of proteinase gene expression but is instead associated with changes in the level of house-keeping gene expression relative to the total RNA pool.

AMINO ACID TRANSPORT (J.Y. Yeh, Bor-Rung Ou, GRAs). A minor component of our research effort is to characterize mechanisms by which nutrients enter muscle cells. Specifically, we have been studying mechanisms by which leucine, an essential amino acid, enters muscle cells. We spent about 2 years characterizing the system and recently made the surprising observation that if you reduce protein synthesis in muscle, leucine transport is increased. Hence, we are proposing that in normal skeletal muscle that there exists a protein which represses transport and when its synthesis is reduced transport is increased. Further studies are planned to characterize the putative repressor in more detail. A grant to the NIH will be submitted in July of 1991 to obtain support for this project.

PROTEIN KINASE C's AND CALPAINS IN THE BOVINE CORPUS LUTEUM (M.A. Ilian, GRA). In collaboration with Dr. Fred Stormshak, we have received a USDA grant to study the biology of oxytocin secretion in the bovine corpus luteum. M.A. Ilian, a graduate student currently working with Neil Forsberg, will be continuing to work on this project as a post-doctoral research associate in the summer of 1991. Because oxytocin secretion from the CL is controlled by protein kinase Cs (PKC) and because proteinases (i.e. calpains) metabolize the PKCs, the project will first characterize PKC and calpain isoforms in this tissue. The project will involve many different techniques in biochemistry, immunology and protein chemistry.