

Concurrent Strength and Endurance Training: From Molecules to Man

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ABSTRACT

NADER, G. A. Concurrent Strength and Endurance Training: From Molecules to Man. *Med. Sci. Sports Exerc.*, Vol. 38, No. 11, pp. 1965–1970, 2006. Strength and endurance training produce widely diversified adaptations, with little overlap between them. Strength training typically results in increases in muscle mass and muscle strength. In contrast, endurance training induces increases in maximal oxygen uptake and metabolic adaptations that lead to an increased exercise capacity. In many sports, a combination of strength and endurance training is required to improve performance, but in some situations when strength and endurance training are performed simultaneously, a potential interference in strength development takes place, making such a combination seemingly incompatible. The phenomenon of concurrent training, or simultaneously training for strength and endurance, was first described in the scientific literature in 1980 by Robert C. Hickson, and although work that followed provided evidence for and against it, the interference effect seems to hold true in specific situations. At the molecular level, there seems to be an explanation for the interference of strength development during concurrent training: it is now clear that different forms of exercise induce antagonistic intracellular signaling mechanisms that, in turn, could have a negative impact on the muscle's adaptive response to this particular form of training. That is, activation of AMPK by endurance exercise may inhibit signaling to the protein-synthesis machinery by inhibiting the activity of mTOR and its downstream targets. The purpose of this review is to briefly describe the problem of concurrent strength and endurance training and to examine new data highlighting potential molecular mechanisms that may help explain the inhibition of strength development when strength and endurance training are performed simultaneously. **Key Words:** EXERCISE, SKELETAL MUSCLE, ADAPTATION, SIGNAL TRANSDUCTION

Adaptations to exercise are highly dependent on the specific type of training performed (4,20,26,35). Endurance training, which represents one extreme of physical activity, generally encompasses exercise durations of several minutes up to several hours at various exercise intensities, increasing the capacity to sustain repetitive high-intensity, low-resistance exercise such as cycling, running, and swimming. This increased ability to perform is mainly accomplished through an increase in maximal oxygen uptake ($\dot{V}O_{2max}$) and an increased ability of skeletal muscle to generate energy via oxidative metabolism without improvements in muscle strength (4,20). Strength training, which represents the other extreme of physical activity, encompasses short-duration activity at high or maximal exercise intensities, increases the capacity to perform high-intensity, high-resistance exercise of a single or relatively few repetitions such as Olympic weightlifting, powerlifting, and throwing events

in track and field. Improved strength-related performance is accomplished through neuromuscular learning and increased fiber-recruitment synchronicity, muscle cell hypertrophy, and, possibly, hyperplasia without changes in $\dot{V}O_{2max}$ or in the capacity to generate ATP via oxidative metabolism (26,27,31). Given such contrasting modes of exercise, and the fact that a large number of sports activities such as sprint running (middle distance), rugby, football, swimming, and the decathlon (among many others) seem to require combinations of both components of strength and endurance training for peak performance, a hypothetical model of a strength–endurance continuum (SEC) can be defined to illustrate the range of strength, endurance, and metabolic combinations that training should stress for improved performance (Fig. 1). As a consequence, training for many of these sports will likely encounter some logistical problems and some possible biological limitations during the course of performance development.

In view of the divergent adaptations induced by strength- and endurance-training regimes and the potential limitations observed when both forms of exercise are performed simultaneously, the main goal of the present review is to briefly describe, based on the existing evidence, whether simultaneously training for strength and endurance results in enhanced or diminished performances that occur when either type of training is performed alone. A second goal is to outline potential physiological, biochemical, and molecular mechanisms associated with

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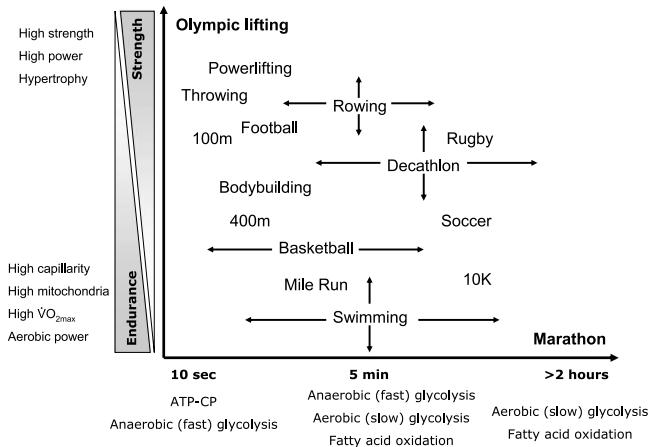


FIGURE 1—The strength–endurance continuum (SEC) is depicted in the context of sports performance and its relation to duration and energy metabolism. From a muscle-energy and training-specificity standpoint, exercise activities of several seconds up to 1 min generally use immediate sources of energy such as ATP, creatine phosphate, and glycolysis and require maximal power and strength. Exercise durations of several minutes in length generally use glycolysis, glucose oxidation, and some fatty-acid oxidation that require near-maximal or maximal $\dot{V}O_{2\max}$ uptake with varying degrees of strength. Long-term exercise from approximately 20–30 min up to several hours in duration use primarily aerobic glycolysis and fatty-acid oxidation at submaximal work rates as close to $\dot{V}O_{2\max}$ as possible, and seem to require a small amount of strength. Although training for sports at the ends of the SEC seems relatively straightforward, a more complicated scenario emerges when designing training programs for those sports requiring combinations of strength and endurance and a mixture of fuel-generating sources.

the responses of skeletal muscle to different forms of exercise that may contribute to the interference of strength development during concurrent training.

INCOMPATIBILITY OF CONCURRENT STRENGTH AND ENDURANCE TRAINING: EFFECTS ON STRENGTH DEVELOPMENT

The goal of the initial study describing the phenomenon of concurrent training was to determine how individuals would adapt to a combination of strenuous heavy-resistance strength and high-intensity endurance training compared with the adaptations produced by either the same strength- or endurance-training regimes separately. This study was published by Robert C. Hickson in 1980 (19) and (intellectually) originated during his postdoctoral studies with Dr. John Holloszy after a running program had been added to his ongoing strength-training regime (Robert C. Hickson, personal communication, 1997).

The following considerations were taken into account in the experimental design: a) both types of training would involve the same muscle groups; b) the response to the endurance and strength programs would not overlap, that is, there would be no increase in strength with endurance training and there would be no increase in $\dot{V}O_{2\max}$ with strength training; and c) the magnitude of change in the criteria variables ($\dot{V}O_{2\max}$ and strength) would be large enough to detect any divergent responses by the groups.

There were three exercise groups: a strength group (S) that exercised $30 \text{ min}\cdot\text{d}^{-1}$, $5 \text{ d}\cdot\text{wk}^{-1}$ for 10 wk; an endurance group (E) that exercised $40 \text{ min}\cdot\text{d}^{-1}$, $6 \text{ d}\cdot\text{wk}^{-1}$ for 10 wk; and a S & E group that performed the same daily exercise regimens as the S group and the E groups combined. For the strength-training programs, all exercises were performed with as much weight as possible. As strength increased, additional weight was continually adjusted throughout training to maintain maximal resistance for the required repetitions. Similarly, for the endurance-training programs, as the subjects' power output increased during training, the cycling work rate also was increased as needed to approach $\dot{V}O_{2\max}$. The running program consisted of continuous running as fast as possible for $30 \text{ min}\cdot\text{d}^{-1}$ during the first week, $35 \text{ min}\cdot\text{d}^{-1}$ during the second week, and $40 \text{ min}\cdot\text{d}^{-1}$ thereafter. In the present study, $\dot{V}O_{2\max}$ was used as the major criterion variable to establish an endurance-training effect. $\dot{V}O_{2\max}$, when measured during cycling or treadmill running and expressed in absolute ($\text{L}\cdot\text{min}^{-1}$) or relative terms ($\text{mL}\cdot\text{kg}^{-1}\cdot\text{min}^{-1}$), increased to the same extent (20–25%) in the E group and in the S & E group. $\dot{V}O_{2\max}$ increased slightly (4%) in the S group during cycling; otherwise, strength training did not result in any other significant changes in $\dot{V}O_{2\max}$ when expressed in either absolute or relative values. As expected, endurance training did not significantly increase strength. Strength training produced increases in strength such that on a weekly basis it was possible to note significant improvement in the parallel squat throughout the 10-wk training program. In contrast, heavy resistance training combined with a program of endurance training produced significant improvement in strength during the first 6–7 wk, followed by a leveling-off period, and then, surprisingly, strength decreased during

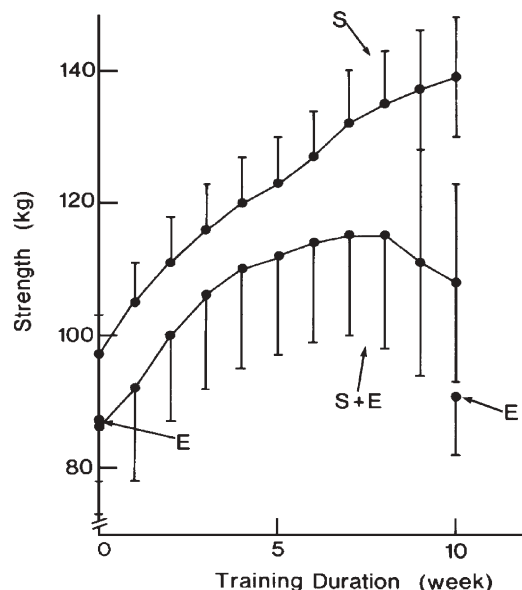


FIGURE 2—Interference of strength development by simultaneously training for strength and endurance as originally reported in the scientific literature. Reproduced from Hickson, R. C. Interference of strength development by simultaneously training for strength and endurance. *Eur. J. Appl. Physiol. Occup. Physiol.* 45:255–263, 1980.

the last 2 wk of the training program (Fig. 2). These results provide the first evidence suggesting that at the upper limits of strength development, endurance training inhibits or interferes with further increases in strength. These results also suggest that there is little relationship between the acquisition of strength and the rate of increase in aerobic power.

Additional studies have confirmed the finding that concurrent training interferes with the development of strength. For example, Dudley and Djamil (13) studied the combination of high-intensity interval cycling endurance training and high-velocity isokinetic strength training. In this study, cycling $\dot{V}O_{2max}$ increased to the same extent (~18%) in both the E and S & E groups when measured several times over the 7-wk period, but strength improvements were different between S and S & E groups. The S group had increases in maximal torque at 0.00–4.19 $\text{rad}\cdot\text{s}^{-1}$, whereas the S & E group had a significant improvement only at 0.00, 0.24, and 1.68 $\text{rad}\cdot\text{s}^{-1}$, suggesting that, in this case, the interference in strength development occurred at high but not low velocity rates of force production. Further evidence demonstrating the interference of strength development by concurrent training was provided by Kraemer et al. (22), who found that combining strength and endurance training affected strength training-induced increases in fiber cross-sectional areas. Such observation suggests that the interference of strength development can also occur at the cellular level. In addition, these authors also found that concurrent training compromised strength development only when both modes of exercise engaged the same muscle group, again suggesting a local effect rather than a systemic one.

Other investigations have reported no inhibition of strength development by concurrent strength and endurance training. For example, Sale et al. (32) trained two groups, one leg in one group completed a strength program and the other leg a strength endurance program. In the second group, one leg was endurance trained and the other endurance and strength trained. Endurance training consisted of five 3-min bouts of cycling at work rates requiring 90–100% $\dot{V}O_{2max}$, whereas strength training consisted of six sets of 15–22 repetitions on the leg press at maximal resistance for a total of 22 wk. All types of training produced similar responses, including increased strength, $\dot{V}O_{2max}$, and vastus lateralis muscle citrate synthase activity. In view of the similarity of responses to these regimens, it is understandable that no inhibition of strength was observed by the combination of training, because the training regimes seem to have been more synergistic rather than antagonistic.

After these initial studies, a number of other investigations either favored or disagreed with the interference of strength development during concurrent training. Many such discrepancies among studies of concurrent training stem from a number of logistical issues. Based on the evidence provided so far, the interference effect seems to hold true in specific situations. Some of the different results were postulated to be related to dependent-variable

selection (outcome measures), modality of training programs, characteristics of the subjects (age, sex, training status), and duration of the study (24). Moreover, such differences make comparisons across the different studies difficult, which complicates the understanding of the adaptations to concurrent training.

POTENTIAL MECHANISMS RESPONSIBLE FOR THE INTERFERENCE OF STRENGTH DEVELOPMENT DURING CONCURRENT STRENGTH AND ENDURANCE TRAINING

Over the years, several mechanisms have been proposed as limiting factors for optimal skeletal muscle adaptation, and have been identified as “responsible” for or contributing to the inhibition of strength development during concurrent training. These include neural components, fuel substrate availability, fiber-type transformation, overtraining, and alterations in protein synthesis (24).

Neural component. Dudley and Djamil (13) and Chromiak and Mulvaney (8) have discussed the possibility that neural factors and motor unit recruitment may have a significant role in restricting strength development with strength and endurance training. However, no specific factors have yet been isolated to strongly support this mechanism, with the exception of a study by Hakkinen et al. (15), in which the effects of concurrent training on rates of force development were postulated to have been a consequence of neural and muscle components, because this type of training attenuated the development of explosive strength by limiting rapid voluntary neural activation.

Low glycogen content. Successive bouts of either strength or endurance exercise may produce chronically low muscle-glycogen levels, which could retard or impair subsequent performances. Repeated endurance training on consecutive days can reduce resting muscle glycogen levels in muscle (9), and glycogen depletion has been shown to occur after resistance exercise (35). A possible implication of low glycogen levels on concurrent training-induced muscle adaptation is highlighted by the findings of Creer et al. (10), who recently reported that low muscle-glycogen levels impaired the intracellular signaling responses to an acute bout of resistance exercise. Therefore, carrying out a training program that entitles daily or even twice-daily sessions may impair the responses to, and recovery from, exercise and/or performance during the execution of subsequent training sessions, thereby reducing the magnitude of the strength-training adaptations.

Fiber-type transformation. Changes in muscle-fiber composition, particularly as a function of isomyosin alterations, have been considered previously as a possible mechanism of endurance training-associated inhibition of strength development (8,14). Skeletal muscle hypertrophy after strength training occurs to a greater extent in fast-twitch than in slow-twitch fibers (16,34). Intense endurance training has been observed to reduce the maximal

shortening speed (\dot{V}_{\max}) of type II or fast-twitch fibers and to change skeletal muscle-fiber population as measured by changes in myosin ATPase (25,33), which suggests that a reduction in the relative number of type II fibers by endurance training could play a major role in limiting strength development during concurrent training.

Overtraining. Two previous reviews (8,14) of concurrent strength and endurance training have considered the term “overtraining” to account for the inability to attain optimal strength gains when strength and endurance training are performed. Overtraining remains a rather poorly defined term despite recent efforts by exercise physiologists to identify its origins. Overtraining is an imbalance between training and recovery (23). In general, it is characterized by a decline in performance or by a lack of improvement. In the first strength- and endurance-training study, strength declined in the 9th and 10th weeks of concurrent training (19). Because the subjects were training $80 \text{ min}\cdot\text{d}^{-1}$, an argument could be made that the marked impairment of strength development by the S & E groups was the result of the development of residual fatigue. Yet, this may not have been the case. Endurance work per week performed on the bicycle ergometer increased at approximately the same rate in the E and S & E groups, particularly during the 9th and 10th weeks of training, at a time when strength gains in the S & E group were dramatically decreasing (Fig. 2). Thus, the S & E effects on strength development seem to be selective for the strength-training response. Furthermore, the studies of Dudley and Djamil (13) and Hickson (19) as well as other concurrent training studies encompassed somewhat different endurance- and strength-training protocols (intensity, duration, frequency, type of training), including the sequence of days when either one or both types of training were performed. Based on these differences, it is difficult to uniquely identify the factor(s) leading to the inhibition of strength by overtraining during both types of training.

Protein turnover. Acute endurance exercise bouts have generally been found to reduce total protein-synthesis rates of mixed skeletal muscles during the exercise. This depression is transient and can lead to a temporary decrease in protein synthesis within several hours after exercise (5,12,29). Overlapping endurance exercise bouts with resistance exercise may result in impaired adaptive responses in protein synthesis and, therefore, a decrease in strength-related performance, in part, due to the suboptimal or lack of increase in muscle-fiber cross-sectional areas (22). When performed several times a week, such combination training may be sufficient to disrupt the protein-synthesis mechanisms involved with the normal adaptation to the individual bouts of strength exercise, thus altering the long-term adaptations to training and resulting in impaired muscle-dependent strength gains. Another possibility, although hypothetical, is that the adaptive protein synthesis resulting from either form of exercise may create some sort of cellular incompatibility in which the muscle cell needs to decide whether to grow or manage the synthesis of its metabolic machinery.

INTRACELLULAR SIGNALING DURING STRENGTH AND ENDURANCE TRAINING: LESSONS FROM MOLECULAR BIOLOGY

We are now at a stage in which technologies from fields such as biochemistry and molecular biology can allow exercise scientists to explore the biology of exercise-induced skeletal muscle adaptation in more mechanistic terms. Studies on protein phosphorylation of intracellular signaling molecules have begun to reveal specific cellular regulatory processes induced by different forms of exercise. For example, acute resistance exercise, which, over time, can result in muscle hypertrophy, induces the activation of a growth-associated signaling network. Experiments in humans and rodents demonstrated that a single bout of resistance exercise results in an increased activity of the phosphoinositide-3-dependent kinase (PI3k) (18), protein kinase B (PKB) (28), the mammalian target of Rapamycin (mTOR) (3), and the ribosomal protein S6 kinase 1 (S6k1) (1,21,28). Activation of such a signaling network by acute resistance exercise modulates muscle-protein synthesis both in animals and humans (18,11). Activation of PI3-k leads to an increase in PKB and mTOR activity and subsequent inhibition (phosphorylation) of the cap-binding protein 4E-BP1 (3,18), which, in turn, inhibits cap-dependent mRNA translation and, hence, protein synthesis via sequestration of the eukaryotic initiation factor 4E (eIF4E). An increase in eIF4E activity will result in increased muscle-protein synthesis rates. Endurance exercise, on the other hand, is associated with signaling mechanisms related to metabolic adaptations, such as the activation of the AMP-activated protein kinase (AMPK) signaling. One of AMPK's main functions is to monitor the energy status of the cell; therefore, the processes regulated by AMPK seem to be related to the maintenance of energy homeostasis (17,37). AMPK activity is modulated mainly by changes in the levels of energy phosphates and by a decrease in the energy charge of the muscle cell, that is, an increase in ADP/ATP ratio. Such fluctuations in metabolic regulation as it occurs during exercise (38,39) can also cause changes in gene expression and substrate content via AMPK signaling (17,37).

Interestingly, recent studies have shown antagonistic activities between the anabolic signaling mechanisms induced by the PI3k/mTOR/PKB/S6k1/4E-BP1 network and the energy-modulating signaling by AMPK. More precisely, activation of AMPK signaling by a pharmacologic agonist reduces skeletal muscle-protein synthesis by inhibiting mTOR signaling, presumably via activation of the tuberous sclerosis complex (TSC). Bolster et al. (2) have found that an injection of the AMPK analog AICAR (5-aminoimidazole-4-carboxamide 1-beta-d-ribo-nucleo-side) had no effect on $\alpha 1$ AMPK activity, but it did increase $\alpha 2$ AMPK activity by ~50%. AMPK activation by AICAR treatment was correlated with a 45% decrease in protein synthesis and was associated with a decreased activation of the PKB/mTOR/S6K1 pathway. This was also associated with a reduced inhibition of the eIF4E-binding

protein (4E-BP1) and a reduction in eIF4E associated with eIF4G. As previously mentioned, one potent stimulus for the increase in AMPK activity is an increase in ADP/ATP ratio; this mechanism may help explain previous observations by Bylund-Fellenius et al. (7), who demonstrated that contractile activity resulted in an increase in ADP/ATP ratio, which, in turn, was correlated with a fall in muscle-protein synthesis rates. These findings indicate that the decrease in protein synthesis commonly seen during contractile activity could be mediated in part by an increase AMPK activity and a concomitant decrease in the anabolic response downstream of mTOR signaling. Indeed, Thomson and Gordon (36) have recently made the interesting observation in aged animals that muscle mass was negatively correlated with AMPK activity, once again implicating this kinase in the negative modulation of skeletal muscle mass.

Another potential mechanism for the inhibition of protein synthesis during muscular activity may be at the elongation step (6). In a recent study, Rose et al. (30) detected a rapid increase in eukaryotic elongation factor 2 (eEF2) phosphorylation during cycling exercise. In this study, subjects exercised at approximately 67% $\dot{V}O_{2max}$, and muscle biopsies were obtained at rest and after 1, 10, 30, 60, and 90 min of exercise. Exercise caused a rapid (within 1 min) increase (five- to sevenfold) in eEF2 phosphorylation that persisted during the entire exercise period. Surprisingly, a rather small decrease in eEF2 kinase (eEF2k) activity was detected, suggesting that even with a minor decrease in eEF2k activity, the remaining activated kinase may have been sufficient to inhibit and, therefore, phosphorylate eEF2, causing a decrease in protein synthesis. The mechanisms by which eEF2k activation by exercise seems to occur in a calcium-dependent fashion, because eEF2k from exercised muscle was potentially activated by calcium-dependent calmodulin (Ca^{2+} CaM) *in vitro*. This suggests that the higher eEF2 phosphorylation in working skeletal muscle may be mediated by an allosteric activation of eEF2 kinase by Ca^{2+} CaM.

SUMMARY AND FUTURE RESEARCH DIRECTIONS

Although hypothetical, it is reasonable to assume that activation of AMPK and inhibition of the eEF2 by endurance exercise and/or too-frequent exercise sessions will impinge on the responses to resistance exercise by affecting training-induced increases in adaptive protein synthesis, because activation/inhibition of these signaling proteins independently or collectively can alter the induction of an anabolic response. The obvious consequence of

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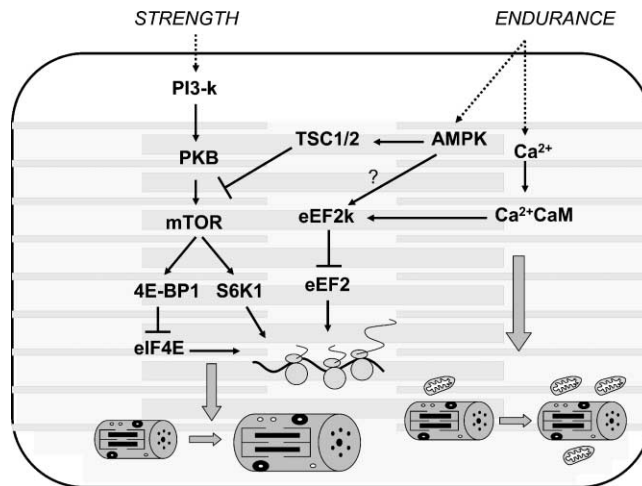


FIGURE 3—A working model of the intracellular signaling networks mediating exercise-induced skeletal muscle adaptations. Resistance exercise is capable of inducing an increase in the activity of a network comprising PI3k/PKB/mTOR/S6K1/S6/4E-BP1 signaling to modulate protein-synthesis rates and muscle growth. Endurance exercise is associated with signaling involved in metabolic homeostasis, comprising AMPK signaling, among others. Activation of AMPK by endurance exercise or contractile activity may inhibit mTOR signaling via TSC and suppress resistance exercise-induced muscle-protein synthesis. In addition, calcium fluxes resulting from prolonged contractile activity may inhibit protein synthesis in a Ca^{2+} M-dependent manner by inhibiting peptide-chain elongation via activation of eEF2k and a subsequent increase in eEF2 phosphorylation. AMPK may also inhibit protein synthesis by activating eEF2k.

such antagonism will be a negative impact on long-term strength-training adaptations, perhaps by ameliorating the hypertrophic response. Therefore, this may be one mechanism responsible for the observed detrimental effects of concurrent strength and endurance training on strength development (Fig. 3).

In summary, when strength and endurance training are performed simultaneously, a potential interference in strength development may occur. Such interference may be caused by alterations in the adaptive protein synthesis changes induced by endurance exercise or by too-frequent training sessions, in addition to several other unknown factors. Novel technologies are allowing us to understand the molecular mechanisms involved in exercise-induced skeletal muscle adaptations (e.g., genome-wide gene-expression analysis). This knowledge is not only improving the way we implement training programs for sports and rehabilitation, it is also important for the correct design of future studies in exercise training and skeletal muscle adaptation, particularly those involving the investigation of mechanisms of signal transduction and gene expression.

The present review is dedicated to the memory of my past mentor, Robert C. Hickson.

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