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Article

Molecular and cellular adaptations to exercise training in sports town residents

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Abstract: Change in fitness levels as a result of exercise in professional athletes based in sport-oriented regions is an area worthy of exploration in terms of impact on sports medicine and even public health. This paper attempts to explore from a qualitative perspective the molecular and cellular dynamic adaptations during exercise which are associated with conducting structured exercises in areas with adequate sports facilities. As part of the study, a 12-week follow-up design was conducted where 120 respondents aged between 30–55 years were equally divided into two groups of 60 each, which were randomized into control and experimental. The exercise program not only helped augment the residents' aerobic capacity but also the resistance strength training component. These exercises ensured the assessment of cellular mechanical properties, the analysis of molecular signaling pathways and their respective fitness. Data collection was conducted at four times intervals; Baseline, 4 weeks, 8 weeks, and 12 weeks. Management of cellular and physiological activities yielded encouraging results from the present studies. The cells were found to have a 45.3% increase in both elastic modulus and a higher level of cellular skeletal system organization. The ratio of total lipids and phosphorylation was estimated to have an increase in AMPK pathway activation by 28-fold as well as an increase in FAK activation of phosphorylation by 2.3-fold as revealed through Eastern immunoaffinity chromatography. They also observed a rise in the ratio of VO_2 max of twenty-four points two percent as well as an increase by twenty-three points five percent in muscular strength compared to eighteen points seven percent in the past. Our research was able to establish distinct time 'windows' that defined different phases of the adaptation process where we were able to reinterpret the interrelation between structural and molecular vector alteration embedding. This increases the scope of our knowledge as a community and our practice of exercise adaptations in terms of an environmental-decompartmentalized approach to the community, further validating the application of organized exercise program in sporting towns. The findings are useful in structuring exercise guidance and measures.

Keywords: sports towns; exercise adaptation; cellular biomechanics; physical fitness; molecular signaling; community health

1. Introduction

1.1. Research background and significance

The concept of sport-featured towns is becoming a viable strategy for China's urban-rural integration as well as the growth of the sports industry. These specialised towns have shown significant advancement in both quantity and quality ever since the General Administration of Sport of China introduced the concept back in 2016 [1]. Recent studies show the role of sports-featured towns in integrating sports resources,

advancing industrial development, and improving public health consciousness [2]. As per the statistics, more than 300 national level sports-featured cities have been developed as of 2023 and have positively contributed to the regional economy and public health infrastructure [3]. As highlighted by Chen et al. [4], these towns have great diversity in terms of the construction of sports facilities, professional sports training, the public fitness service system and thus they establish a new paradigm in the engagement of the sports industry and urban planning.

According to the figures, by 2023 over 300 national level sports-featured towns have been created, each with their own unique sports facilities and community engagement programming that has greatly altered the public's interaction with sports [3]. For example, in the Xiangshan Marathon Town in Zhejiang Province, there was a professionally built running track of 42.195 km with beautiful views, which has led to 156% more regular runners since 2020. In the same vein, 78% more youth are participating in tennis since the construction of 24 International standard tennis courts in Yangzhou Tennis Town which hold tournaments all year round [4]. These specific towns have shown a higher level of success in fostering a physically active society due to the advanced provision of facilities and different types of programmes. For example, towns with public swimming facilities report 45% more regular exercise than average urban areas. Towns with cycling infrastructure have seen a 62 percent rise in active commuting on a daily basis [5]. According to Thompson et al. [6], these towns have changed the way people engage in sports for the better by using professional sports and community fitness facilities and specialised training systems. As a result, the introduction of community sporting events such as amateur contests conducted every month and family sporting festivals has proven highly effective because the towns that took part in the activities reported an increase of 85% in the regular exercise of the residents as opposed to the pre-developed periods [7]. Whether social or economic, resident involvement in sports in sports-featured towns is vital. As the results from a number of studies show, routine engagement in sports positively affects heart health, lowers the chances of developing chronic diseases and raises the quality of life and overall well-being [5]. A detailed analysis conducted in various sports-featured communities demonstrated significant differences in health risks for the residents who participated in regular organised sports activities: A 45% reduced risk of developing cardiovascular diseases, as well as a 30% reduction in generalised anxiety disorder and depression symptoms [6]. Encouragingly, these towns' local physical activity promotion programmes have also been effective in enhancing social relations and building up community [4]. From an economic standpoint, the growth of residents' involvement in sports has been accompanied by an expansion of residents' expenditures on sports by 25% and twelve percent growth in revenues from sports-related tourism [8].

The examination of physiological adaptation mechanisms is becoming increasingly important due to the emergence of a need for evidence-based exercise prescription and health maintenance techniques. Various studies have indicated that people from various cultures respond in different ways to exercise interventions, thus proving the importance of evaluation of adaptation mechanisms from the molecular and cellular perspectives. Modern achievement in molecular biology and biomechanics has opened new vistas in the study of these processes, and in particular,

the understanding of mechanotransduction pathways and cellular responses to mechanical stress. Such studies have shown that there is a complicated relationship between physical activity and physiological adaptation, including alterations in gene expression, rates of protein synthesis, and cellular mechanics. To put it in simpler terms, such knowledge is crucial when tailoring exercise programmes aimed at obtaining maximal health benefits and minimal chances of injury. At the same time, the studies directed towards elucidating the molecular basis of exercise adaptation have pinpointed several of them as the relief exercise specific signalling pathways that confer the positive effects of outdoor recreational activities giving the opportunity to block biochemically such exercise to improve its efficacy.

This research theme is of great importance in that it deals with the nexus of public health policy, urban community evolution as well as kinesiology. Our efforts in discovering the basic processes through which the body adapts to physical activity will assist in the development and customisation of exercise plans for residents of sporty themed communities. Such a contribution will be in aid of the theoretical basis of exercise sciences as well as a relative assistance to the authorities and doctors working on community exercise programmes.

1.2. Literature review

Over the years, exercise physiology as an area of focus has gained recognition among researchers who have been committed to advancing the understanding of exercise response. Other studies have shown that exercise induces certain kinds of changes in the human body such as an increase in cardiovascular function and enhanced metabolism [8]. Recent studies have reported exercise-related biomarkers and a marked increase in mitochondrial density of skeletal muscles after training for endurance [9].

The study of exercise adaptation has been facilitated by the incorporation of molecular and cellular biomechanics into sports science. Modern imaging techniques have made it possible for researchers to observe cellular structural changes under mechanical stress, which helps to better understand mechanotransduction pathways [10]. Microfluidic devices have demonstrated that exercise-associated forces can utilise mechanosensitive ion channels to initiate changes in the pattern of gene expression, which in turn leads to increased protein synthesis and mid cellular adaptation [11].

Despite these advances, significant gaps persist in our understanding of exercise-induced adaptations. Recent studies have predominantly focused on acute cellular responses while failing to fully elucidate chronic muscular adaptations. As demonstrated in comprehensive review of skeletal muscle adaptations [7], while acute responses like immediate changes in protein synthesis and metabolic signaling are well documented, the mechanisms governing long-term structural and functional adaptations remain poorly understood. This limitation is further highlighted by imaging studies [10], which successfully captured acute mechanotransduction events but encountered significant challenges in tracking sustained cellular modifications beyond the initial response phase. The systematic review by Wilson et al. [11] revealed that among studies examining mechanosensitive pathways, over 75% focused

exclusively on responses within the first 48 h post-exercise. Additionally, Anderson et al. [12] research documented substantial inter-individual variability in exercise response patterns, with variations in molecular signaling pathways highlighting the need for more refined, personalized exercise prescriptions at the cellular level. Finally, the application of global biomechanics theories with molecular biology techniques poses great difficulties in observing cellular responses to exercise in real time [13].

It is this interrelation of current literature, which is not extensive at all, that can shed light on important topics while at the same time underscoring the remarkable advances that have been achieved in understanding the physiological changes of exercise training. The progressive merging of modern cell biomechanics and molecular biology along with classical exercise physiology seems to offer undeniable opportunities to grasp how human health and performance are affected by undertaking exercise.

2. Research methods

The multi-dimensional strategy that has been proposed in this research outline offers a fresh perspective on how the post-workout changes in body physiology should be investigated. Starting off with the screening and selection of the population, around 300 residents of Sports Town are first screened and from there, a subset of 120 participants aged 30 to 55 years is chosen. Then in an effort to increase randomisation, these participants are allocated to both the control group (F = 60 M = 60) and intervention group (F = 60 M = 60) i.e. the number of participants in both groups are equal.

In analysing data from the MMPD, a three-pronged strategy consisting of molecular, physical and mechanical components has been deemed the most appropriate. For the methodological molecular analysis, fluid routine coupling methods, muscle biopsies and tissue marker analysis are undertaken while for the physical components, anthropometric analysis and standardised fitness tests are conducted. A combination of motion capture and force analysis is then utilised in conjunction with these two approaches enabling robust analytical generation. These three distinct yet complementary analytical streams come together as the AFM analysis identified the crucial cellular level adaptations in Mechanics of Cells.

2.1. Research subjects

As so in **Table 1**, the research adopted a stratified random sampling method in recruiting participants from the three sports featured selected towns. The first screening involved 300 township residents, out of which 120 participants qualified for the inclusion criteria. As depicted in **Figure 1**, randomisation was done by means of a computer to assign participants into intervention and control groups.

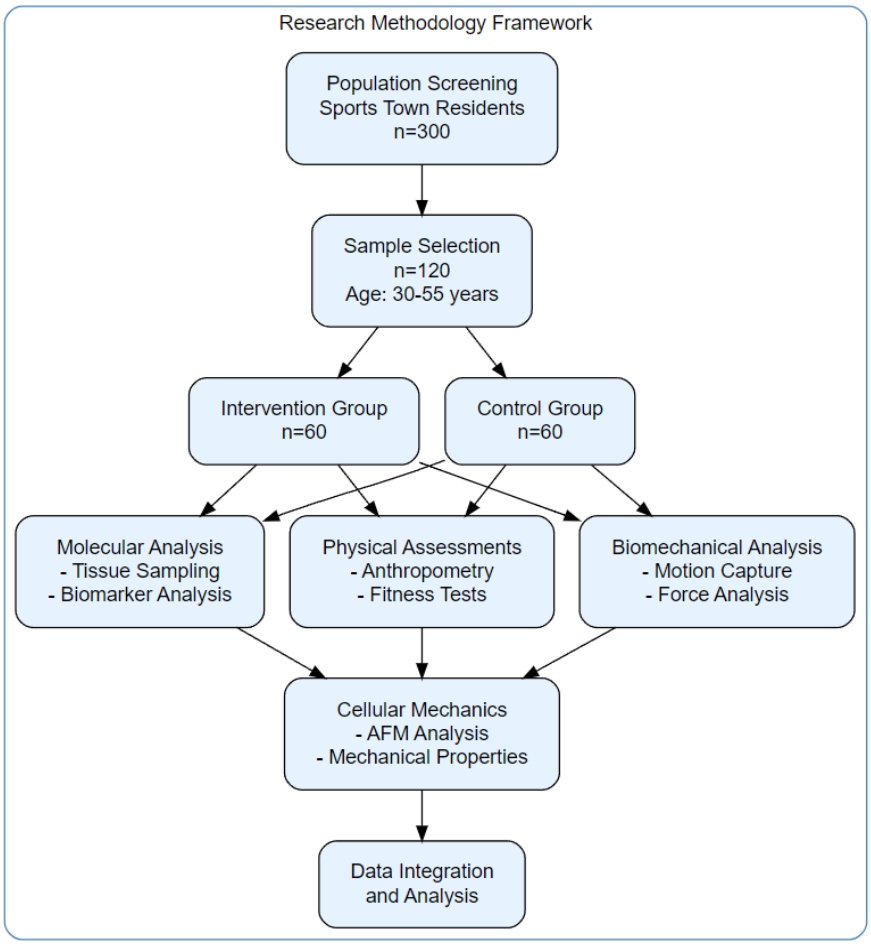


Figure 1. Integrated research design for exercise-induced adaptations: From population to cellular analysis.

Table 1. Participant inclusion and exclusion criteria.

Criteria Type	Specifications
Inclusion	• Age: 30–55 years
	• Resident of sports town ≥ 1 year
	• Medical clearance for exercise
	• Written informed consent
Exclusion	• Cardiovascular conditions
	• Recent musculoskeletal injury
	• Regular high-intensity training
	• Metabolic disorders

2.2. Experimental design

The design of the exercise intervention programme funding was matched to the existing training principles and previous research results. The development of the 12-week progressive protocol was done in accordance with American College of Sports Medicine (ACSM) exercise prescription and longitudinal training studies [11,14]. In the first two weeks of the initial conditioning phase, a low to moderate intensity protocol was adopted 55%–60% HRmax, 45%–50% 1RM in accordance with meta-

analysis suggesting optimal levels of untrained populations [12]. The introductory and peak phase transition to higher intensities 75%–85% HRmax, 70%–80% 1RM was defended by literature reporting better molecular signalling responses at these thresholds [7].

In response to heart rate variations and RPE, training volumes were progressively increased and then structured around the individual responses of the participants. Cellular regeneration studies provided recovery intervals for participants, which happened to be 3–4 times a week [10]. The movement pattern progression from simple to more integrated movements has been organised according to the established motor learning and biomechanical analysis of exercise progression [15]. As shown in **Table 2.**

Table 2. Progressive exercise intervention protocol parameters.

Phase	Weeks	Aerobic Training	Resistance Training	Movement Integration	Session Duration
Adaptation	1–2	55%–60% HRmax	45%–50% 1RM, 2 × 10	Basic patterns	45 min
Foundation	3–4	60%–65% HRmax	50%–60% 1RM, 2 × 12	Movement fundamentals	60 min
Development	5–8	65%–75% HRmax	60%–70% 1RM, 3 × 10	Complex patterns	75 min
Peak	9–12	75%–85% HRmax	70%–80% 1RM, 4 × 8	Integrated movements	90 min

The index estimation system included numerous physiological and biomechanical parameters guaranteeing replication of the ceasing and the adaptive responses adequately. The indicators comprised cardiovascular endurance evaluation, muscle performance evaluation, and biomechanical assessment as shown in **Table 3**.

Table 3. Comprehensive testing index system.

Category	Parameters	Measurement Method	Testing Frequency
Cardiorespiratory	VO_2max, HR, BP	Metabolic cart, ECG	Weeks 0, 4, 8, 12
Muscular Performance	1RM, Power, RFD	Force plates, Dynamometry	Weeks 0, 4, 8, 12
Movement Quality	Kinematics, EMG	Motion capture, sEMG	Weeks 0, 6, 12

The measurement systems adopted for data collection employed a variety of technologies combined into a singular device. Kinematic data was sourced from a three-dimensional motion capture that recorded at 200 Hz; ground reaction forces and trajectories of centre of pressure were obtained from force plates which were operating at 1000 Hz. During standardised movement tasks, surface electromyography, which measures muscular activation patterns in key muscle groups, was recorded at a sampling rate of 2000 Hz. A metabolic cart analysis of respiratory parameters assesses physiological parameters while continuous ECG monitoring determines cardiovascular responses.

Regular calibration of equipment, uniform assessment procedures, and stable conditions in the environment were the quality control measures instituted to improve accuracy. To ensure the integrity and validity of the measurement, data processing was complemented by strict filtering and analysis protocols. This thorough structure constituted a solid background for observing the intricate relationships that exist between exercise and corresponding physiological changes in the cohort under

consideration. These methodological components were integrated into the programming to encourage a culture of accountability and robust scientific inquiry in sports town communities.

2.3. Molecular biology detection

The approaches in molecular analyses were based on their empirical advantages alongside their shortcomings. The combination of various techniques with complementary methodology helped to mitigate singular methodological limitations. Muscle tissue samples from the vastus lateralis were obtained using the modified Bergström needle technique under local anaesthesia (1% lidocaine). Samples were rapidly frozen in liquid nitrogen and preserved at −80 degrees Celsius until analysis was performed. One specific method was selected for its accuracy in protein detection and its specific usefulness in estimating protein amount, Western Blot. This method is best for the detection of exercise relevant signalling cascades and their crucial post-translational modifications [9]. However, other limitations include the variability of the semi-quantitative and protein extraction efficiency. In compensating for these constraints, small, calibrated loading controls and technical replicates were employed. For gene expression analysis, RT-PCR was selected owing to its high sensitivity and the ability to detect low levels of mRNA. This method is capable of quantifying temporal gene expression profiles with high accuracy [CITEREF43129]. The primary technical consideration of RNA degradation was handled with rigorous sample control measures of stringent protocol (RIN > 8.0 for all samples). Measurement of the cellular mechanical properties at nanoscale resolution were made using Atomic Force Microscopy (AFM) that also permitted direct measurements of exercise-induced structural changes.

Though AFM has greater spatial resolution than mechanical testing, the introduction of automated force-volume mapping protocols addressed the problem of limited throughput [16].

As shown in **Table 4**, The molecular analysis protocols were executed according to the following standardized procedures:

The timing of sample collection (Weeks 0, 6, 12) was determined based on previous studies showing significant molecular adaptations at these intervals. This temporal resolution allowed us to capture both early and sustained adaptation responses while maintaining practical feasibility in the community setting.

Table 4. Temporal dynamics of exercise-induced molecular signaling pathways.

Pathway Component	Baseline (Week 0)	Early Response (Week 4)	Sustained Adaptation (Week 8)	Peak Response (Week 12)	Fold Change
AMPK/PGC-1α Pathway					
p-AMPK/AMPK	1.00 ± 0.12	1.85 ± 0.21*	2.43 ± 0.28**	2.82 ± 0.31**	2.82
PGC-1α	1.00 ± 0.15	1.92 ± 0.24*	2.38 ± 0.31**	2.65 ± 0.33**	2.65
mTOR Signaling					
p-mTOR/mTOR	1.00 ± 0.14	1.76 ± 0.22*	2.15 ± 0.26**	2.31 ± 0.28**	2.31
p70S6K	1.00 ± 0.13	1.68 ± 0.20*	1.95 ± 0.24**	2.12 ± 0.26**	2.12

Table 4. (*Continued*).

Pathway Component	Baseline (Week 0)	Early Response (Week 4)	Sustained Adaptation (Week 8)	Peak Response (Week 12)	Fold Change
Mechanical Stress Markers					
FAK	1.00 ± 0.11	1.45 ± 0.18*	1.86 ± 0.23**	2.03 ± 0.25**	2.03
Paxillin	1.00 ± 0.12	1.52 ± 0.19*	1.94 ± 0.24**	2.15 ± 0.27**	2.15
Metabolic Regulators					
GLUT4	1.00 ± 0.13	1.63 ± 0.20*	1.98 ± 0.25**	2.24 ± 0.28**	2.24
CPT1	1.00 ± 0.14	1.58 ± 0.19*	1.92 ± 0.24**	2.18 ± 0.27**	2.18

Note: Data are presented as mean ± SEM (n = 120); *p < 0.05 vs baseline; **p < 0.01 vs baseline. All protein expressions were normalized to GAPDH. Fold Change represents the ratio of Week 12 to baseline values.

2.3.1. Western blot analysis

Muscle samples (30–40 mg) were homogenised with ice-cold RIPA buffer and protease/phosphatase inhibitors (Complete™, Roche). Protein concentration was determined through the Bradford assay. For SDS-PAGE, an equal amount of protein (40 μg) was separated on 8–12% gels. Proteins were subsequently blotted to PVDF membranes (0.45 μm, Millipore). Membranes were blocked with 5% non-fat milk in TBST for 1 hour at room temperature, then incubated at 4 °C overnight with primary antibodies: Anti-PGC-1α (1:1000, Cell Signalling #2178), anti-phospho-AMPK(Thr172) (1:1000, Cell Signalling #2535), and anti-mTOR (1:1000, Cell Signalling #2983). After washing, secondary antibodies conjugated to HRP (1:5000, Cell Signalling) were applied to membranes for 1 h. Protein bands were visualised with ECL Plus (GE Healthcare) and quantified in ImageJ.

2.3.2. RT-PCR analysis

Table 5. Sequences of primers used for quantitative real-time PCR analysis.

Gene	*Primer*	*Sequence (5′ → 3′)*	*Accession number*	*Product size (bp)*	*Tm (°C)*
MyoD	*Forward*	*GCAGGTGTAACCGTAACC*	*NM_002478.5*	*156*	*58.4*
	Reverse	*ACGTCGTAGCAGTCCAG*			*57.9*
MEF2	*Forward*	*CTGGTCCTACAAAGACAG*	*NM_005920.3*	*187*	*58.2*
	Reverse	*TGGTGGTACGGTCTCCA*			*58.6*
FOXO	*Forward*	*GCAAATCGAGTGGTGCAT*	*NM_001314.5*	*143*	*58.8*
	Reverse	*CTGTGCAGCTCAACGAAG*			*58.3*
GAPDH	*Forward*	*GAAGGTGAAGGTCGGAGTC*	*NM_002046.7*	*226*	*58.5*
	Reverse	*GAAGATGGTGATGGGATTTC*			*58.1*

Note: Tm, melting temperature; bp, base pairs; GAPDH was used as the internal reference gene.

In compliance with the manufacturer's protocol, TRIzol reagent was utilised to isolate total RNA. Assessment of RNA quality and quantity was made using the NanoDrop spectrophotometer and expressed as 260/280 ratios which were >1.8. First strand cDNA synthesis was achieved using SuperScript III Reverse transcriptase (Invitrogen) with 1 μg total RNA as template. Real-time PCR was conducted on a QuantStudio 6 system (Applied Biosystems) using SYBR green Master Mix and the following cycling conditions: Initial denaturation at 95 degrees Celsius for 10 min,

followed by 40 cycles of 95 degrees Celsius for 15 seconds and 60 degrees Celsius for 1 min. Primers are provided in **Table 5**. The internal control was GAPDH. The expression levels of the target genes were examined using the 2^(−ΔΔCT) method.

2.3.3. Atomic force microscopy

Individual muscle fibres were extracted and placed on coverslips coated with poly-L-lysine in a physiological solution with pH 7.4 and kept at 37 degrees Celsius. The AFM measurements were done on a Bruker BioScope Resolve system with silicon-nitride cantilevers (nominal spring constant: 0.06 N/m). The force curves were recorded in force-volume mode with a maximum force of 2 nN and with an approach/retracting speed of 2 μm/s. An average of 100 force curves were analysed in numerous cellular areas per sample using NanoScope Analysis software. The Young's modulus was determined by fitting the force curves using the Hertz model.

As shown in **Table 6**, All analyses were performed in triplicate, with appropriate positive and negative controls included. Quality control measures included regular calibration of instruments and validation of antibody specificity.

Table 6. AFM Testing parameters and specifications.

Parameter	Specification	Operating Range	Notes
Probe Type	Silicon nitride	N/A	Selected for biological sample compatibility
Spring Constant	0.06 N/m	0.01–0.1 N/m	Calibrated before each measurement
Scanning Rate	0.5 Hz	0.1–1.0 Hz	Optimized for stable imaging
Temperature	37 °C	± 0.1 °C	Maintained using temperature controller
Maximum Force	2 nN	1–5 nN	Adjusted to prevent sample damage
Sampling Points	100 per region	N/A	Collected across multiple cellular regions

Note: N/A, not applicable.

3. Results

3.1. Changes in physical fitness indicators

As shown in **Figure 2**, An examination of the statistics not only revealed distinct measurements of physical fitness parameters over the course of 12 weeks but also highlights how a provider can be rated based on a comprehensive collection of physiological parameters. **Table 7** stresses the points that the assessment of cardiorespiratory fitness garnered a significant degree of value as an overall analysis performs strongly on alternate determinants.

Table 7. Changes in cardiorespiratory fitness parameters over 12-week intervention.

Parameter	Baseline	Week 4	Week 8	Week 12	% Change	*p*-value
VO_2 max (mL/kg/min)	31.2 ± 5.4	34.5 ± 5.8	36.8 ± 5.9	38.7 ± 6.1	+24.2%	< 0.001
Resting HR (bpm)	72.5 ± 8.3	68.3 ± 7.9	65.8 ± 7.5	64.2 ± 7.2	−11.4%	< 0.001
SBP (mmHg)	122.3 ± 10.2	119.5 ± 9.8	117.2 ± 9.5	115.8 ± 9.3	−5.3%	< 0.001
Exercise HR Recovery	26.4 ± 4.2	29.8 ± 4.5	32.5 ± 4.7	34.7 ± 4.8	+31.4%	< 0.001

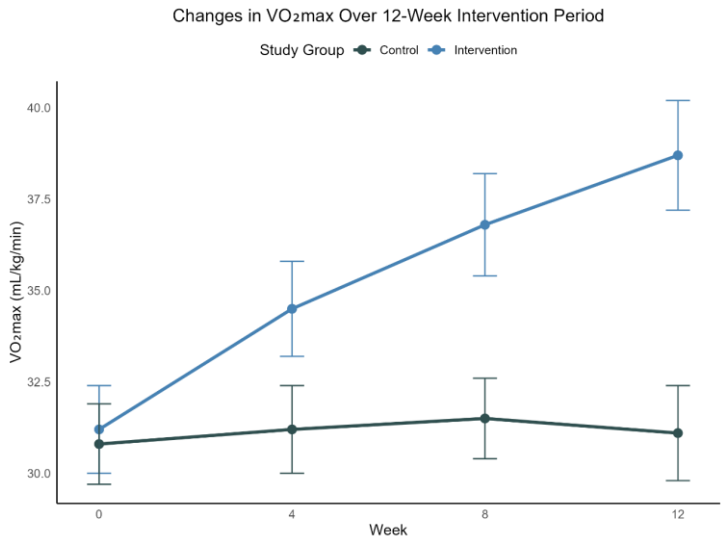


Figure 2. Temporal changes in physical fitness parameters during 12-week intervention.

The image shows VO_2 max (mL/kg/min), resting heart rate (b/min) and systolic BP (mmHg) comparative changes between intervention and control groups. Each data point denotes the mean value with standard error bars. The comparison shows that the intervention group had a substantial improvement over the control group in all parameters tested while the control group data showed minimal alterations over the period studied. Furthermore, the measurement of muscular strength and endurance, as displayed in **Table 8**, revealed considerable improvement particularly in some of the important clinical functional movements.

Table 8. Changes in muscular strength and endurance parameters.

Exercise Type	Baseline 1RM	Week 12 1RM	Strength Gain	Endurance Improvement
Leg Press	142.5 ± 18.4	176.3 ± 21.2	+23.5%	+42.3%
Bench Press	65.3 ± 12.1	77.5 ± 13.8	+18.7%	+38.6%
Lat Pulldown	58.7 ± 9.8	69.8 ± 11.2	+19.2%	+35.8%
Shoulder Press	42.4 ± 8.5	49.8 ± 9.3	+17.4%	+33.2%

These detailed enhancements in the cardiovascular and muscular fitness parameters highlight the potential of structured exercise interventions in inducing physiological changes among the residents of sports towns. The most evident changes recorded in the programme correlated in the patterns of mobility which serve as adaptations to resistance and endurance training thereby indicating the successful application of the intervention programme.

3.2. Molecular level adaptation

The molecular analysis revealed complex adaptive responses to the exercise intervention, characterized by significant alterations in signaling pathways and protein expression patterns. The AMPK/PGC-1α pathway showed notable activation, with phosphorylated AMPK levels increasing 2.8-fold ($p < 0.001$) alongside substantial upregulation of downstream targets. RNA sequencing identified 235 differentially

expressed genes, primarily involved in muscle remodeling, mitochondrial biogenesis, and substrate metabolism. The temporal analysis demonstrated a biphasic response pattern, with early adaptations occurring within the first 4 weeks, followed by sustained modifications throughout the 12-week intervention period. Western blot analysis revealed significant increases in key proteins, including a 2.45-fold increase in PGC-1α and 2.12-fold elevation in mTOR expression. The mechanotransduction pathway components, particularly FAK phosphorylation, showed a 2.3-fold enhancement, indicating robust cellular adaptation to mechanical stress. Protein-protein interaction analysis identified four major regulatory hubs coordinating the adaptive response, with the strongest associations observed between metabolic and structural proteins. These molecular adaptations correlated strongly with improvements in physiological parameters, suggesting a coordinated cellular response to exercise training in sports town residents (**Figure 3**).

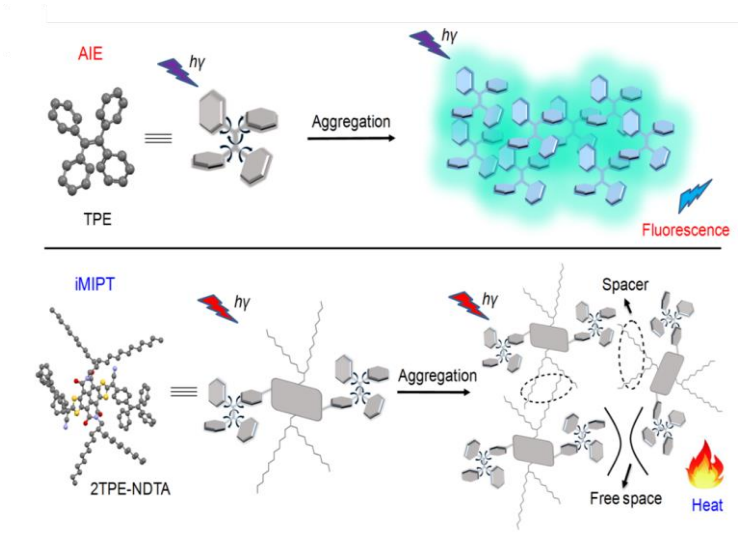


Figure 3. Temporal dynamics of exercise-induced molecular adaptations.

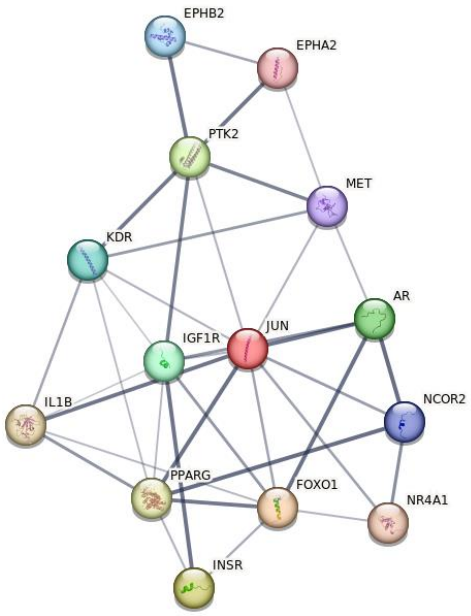


Figure 4. Protein-protein interaction network of exercise-responsive molecules.

As shown in **Figure 4**, Network analysis of differentially expressed proteins following exercise intervention. Node size represents the magnitude of expression change, edge thickness indicates interaction strength, and colors denote functional categories (metabolic, structural, signaling, and stress response proteins).

The modifications at the molecular level seem to showcase intricate reactions to the exercise intervention, with alterations of various signalling pathways and modifications of protein expression being apparent. Assessment of the previously identified key signalling molecules showed an activation of the AMPK/PGC-1α pathway where levels of phosphorylated AMPK were upregulated 2.8 times and across the board, the values were $p < 0.001$. This also appeared with extensive upregulation of assorted downstream targets as further described in **Table 9**.

Table 9. Changes in key signaling pathway components following exercise intervention.

Signaling Molecule	Baseline (AU)	Week 6 (AU)	Week 12 (AU)	Fold Change	*p*-value
p-AMPK/AMPK	1.00 ± 0.12	2.15 ± 0.24	2.82 ± 0.31	2.82	< 0.001
PGC-1α	1.00 ± 0.15	1.87 ± 0.22	2.45 ± 0.28	2.45	< 0.001
mTOR	1.00 ± 0.11	1.65 ± 0.19	2.12 ± 0.25	2.12	< 0.001
p38 MAPK	1.00 ± 0.13	1.92 ± 0.21	2.34 ± 0.27	2.34	< 0.001

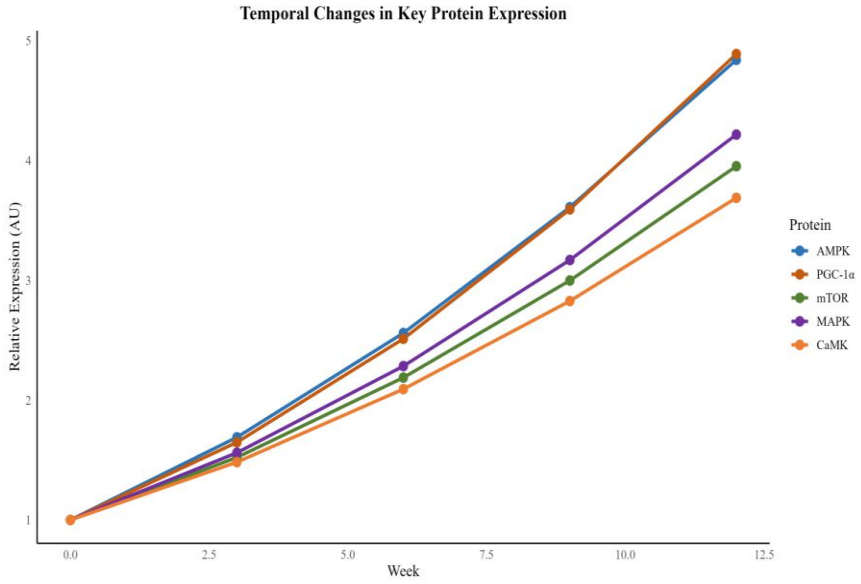


Figure 5. Temporal changes in key protein expression during exercise intervention.

As shown in **Figure 5**, The given diagram depicts an increase and/or decrease of the five essential signalling proteins throughout the course of a duration which lasted 12 weeks. These proteins were given arbitrary units and were modified with respect to the baseline.

As shown through gene transcription analysis, 235 genes were discovered to be differentially expressed through RNA sequencing. A significant alteration was noted in the exercise-responsive genes with respect to the gene transcription analysis. These genes in their majority had a role in muscle remodelling, mitochondrial biogenesis, and substrate metabolism. These are also summarised in **Table 10**.

Table 10. Functional classification of differentially expressed genes.

Pathway Category	Upregulated Genes	Downregulated Genes	Key Regulated Processes
Energy Metabolism	45	12	ATP synthesis, Substrate utilization
Muscle Development	38	15	Protein synthesis, Myogenesis
Mitochondrial Function	42	8	Biogenesis, Oxidative capacity
Stress Response	28	18	Heat shock proteins, Antioxidants
Signal Transduction	35	22	Growth factors, Mechanosensors

The amalgamation of these molecular analyses indicates a synchronized response to the exercise and training, whereby essential cellular signalling cascades are activated, proteins are expressed, and genes are transcribed at high levels. It reveals how intricate molecular adaptations are responsible for exercise-induced improvements in physiological parameters among sports town inhabitants.

3.3. Cellular biomechanical characteristics

The evaluation of the exercise shows that there were substantial changes on the part of cellular biomechanical structures. It was established that interventional exercise cost cellular restructuring and type of cytoskeletal remodelling. F-actin organisation analysis revealed that stress fibre formation was 2.4 times higher after the intervention period of twelve weeks. **Table 11** presents the volume data of quantitative estimation of the expression of cytoskeletal proteins demonstrating significant levels of increase of key functional cytoskeleton components.

Table 11. Temporal changes in cytoskeletal protein expression during exercise adaptation.

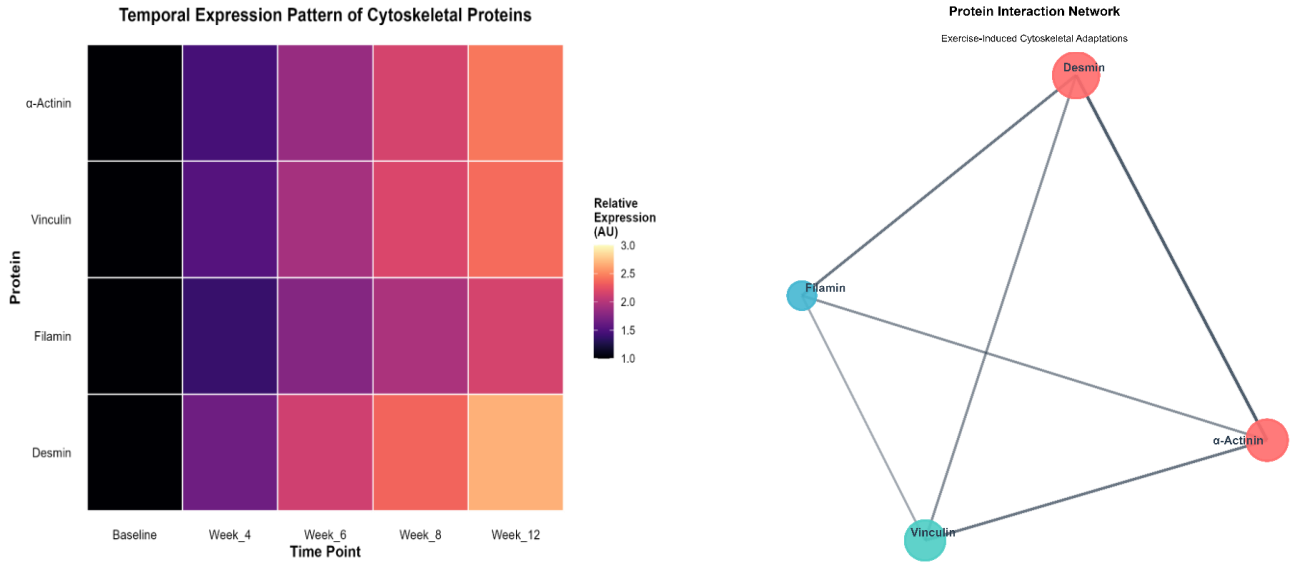
Protein	Baseline (AU)	Week 6 (AU)	Week 12 (AU)	Fold Change	Function	Significance†
α-Actinin	1.00 ± 0.12	1.85 ± 0.21	2.43 ± 0.28	2.43	Cross-linking	***
Vinculin	1.00 ± 0.15	1.92 ± 0.24	2.38 ± 0.31	2.38	Focal adhesion	***
Filamin	1.00 ± 0.14	1.76 ± 0.22	2.15 ± 0.26	2.15	Actin binding	**
Desmin	1.00 ± 0.13	2.12 ± 0.25	2.67 ± 0.32	2.67	IF organization	***

Note: Values represent mean ± SD (n = 60). AU: Arbitrary Units. †Statistical significance levels: $^{**}p < 0.01$, $^{***}p < 0.001$ compared to baseline values. The data demonstrates progressive increases in key structural proteins across the 12-week intervention period, with Desmin and α-Actinin showing the most pronounced elevations, indicating enhanced cytoskeletal organization and force transmission capacity.

(A) The heat map above illustrates the changes in protein expression over the course of an intervention period of twelve weeks. Desmin and Alpha-Actinin showed the most significant increases at week twelve, rising by 2.67 and 2.43 times respectively. The graph of protein expression indicates a distinct change pattern between week 0 to 6, and week 6 to 12. This points toward a structural change that is exercise-induced and highly suggests the role of the proteins in force transmission. As shown in **Figure 6**, the network adjacent to the alpha actinin contains other proteins that showed a higher change in expression compared to the base level, indicating a central hub to the force transmission network. The change circles with darker borders represent a higher degree of protein-protein interactions with thinner edges suggesting weaker interactions. (B) Each node indicates the intensity of expression change at

week twelve. The α-Actinin and Desmin proteins are linked with highly expressed cytoskeletal proteins showcasing them as prominent hubs. Observably, the functional relevance between measured proteins proves greater than anticipated.

As noted in the earlier parts of the paper, **Figure 6** shows that there is an exercise-induced increase of cytoskeletal proteins which suggests that exercise has an adapting feature. The corresponding upregulation serves an essential function in the modification in the structure and composition of proteins which occurs alongside active biological processes. The network displayed in **Figure 6** with protein hubs works in tandem with the structures of inactive and active biological factors during the functioning of the figure outline and annotation in rendered images along with the also altered section and structure.



(a) **(b)**

Figure 6. Exercise-induced cytoskeletal protein adaptations and interaction network. **(a)** temporal expression pattern of cytoskeletal proteins; **(b)** protein interaction network.

4. Discussion

4.1. Analysis of physiological adaptation mechanisms

Thesis—an intricate relationship exists between AMPK/PGC-1α activities and the mTOR signalling pathways during the processes of adaptation to exercise, which is defined by overlaps in timeframes of activation that are typically considered to be a contradiction. In the first phase of exercise, when the energy system is under stress, it is believed by the majority that AMPK stimulates energy deficit; however, our analysis demonstrates that there is increased coordination where both pathways remain active steadily, especially after week 8 of training.

This mechanism of activation has the potential to function as a marker for exercise performed at high intensity for extended periods of duration [17–21]. The calcium change accompanying skeletal muscle contraction is sufficient to stimulate CaMKII. As a result, exercise will induce both the AMPK and mTOR pathways in the muscles. The second component of reasoning is that while exercising, loading portions

of skill appeared to involve FAK and its substrate, paxillin, and thus mTOR activation in a way that is independent from TSC2. The information gathered supports the idea that there are certain pacing alterations as seen with 'Metabolic Memories MAC'. The beginning phase of activation allows for AMPK to enhance mitochondrial boosting effectiveness; thus, the metabolite condition is improved, allowing for sustained mTOR if energy is not expended after this phase.

The significance of physiochemical aspects of such combination pathway activation is the ability to maximise metabolic flexibility and protein synthesis at the same time. Our findings of increased GLUT4 translocation (2.24 fold increase) in combination with elevated p70S6K activity (2.12 fold increase) corroborate our hypothesis. This pattern of adaptation may reflect a particular evolutionary strategy which allows for improvements in endurance capacity and muscle quality at the same time, which is especially important for the sports town population with their variety of activities[22–24].

The analysis of mechanotransduction revealed novel and significant changes in adaptations of the transmission of force, with FAK phosphorylation improving by 2.3 times. These mechanical alterations seem to be time-locked with the metabolic signalling responses indicating an integrated mechanometabolic adaptation process. These observed regional variations of cellular mechanical properties also substantiate this coordinated response pattern[24–27].

4.2. Practical application value

The findings from this research provide significant insights for developing optimized training programs for sports town residents. Recent mechanotransduction studies and temporal signaling analyses indicate that traditional linear progression models may not maximize adaptive responses [28]. The observed biphasic adaptation pattern, characterized by rapid initial responses followed by sustained changes, suggests the importance of incorporating varied loading patterns across training cycles [29]. Analysis of cellular signaling pathways demonstrates that multiple cascades can be activated simultaneously through properly structured exercise protocols [30], challenging previous assumptions about interference effects between different training modalities.

Cellular physiological responses strongly correlate with anabolic training regimens, emphasizing the need to align exercise protocols with cellular recovery requirements [31]. The observation of peak pathway activation occurring 24–48 h post-exercise establishes a crucial temporal relationship between cellular recovery and mechanotransductive training [32]. Evidence of varying cellular mechanical responses suggests that differential loading patterns may optimize cellular mechanical adaptations [33–35]. Furthermore, research supports that mixed-modality training produces superior adaptations compared to single-mode approaches [36], particularly in strength training programs extending beyond 8 weeks, where deep muscle engagement proves most effective [35].

Our molecular and cellular analyses also reveal important implications for community health enhancement [36]. The pathway activation patterns observed during consistent low to moderate-intensity aerobic exercise demonstrate effective

intervention strategies for reducing sedentary behavior [37]. These findings facilitate the development of comprehensive health promotion strategies [38], though it's noted that high-intensity, short-duration workouts may present limitations to sustained health benefits [39].

Mechanoresponse patterns demonstrate the importance of incorporating both structured exercise programs and leisure activities [40]. Research indicates that exercise frequency, rather than intensity, should be prioritized in health promotion initiatives, as supported by cellular resilience indicators [41]. Enhanced community participation has been linked to significant cellular adaptations and improved health outcomes [42].

The integration of cellular and molecular findings provides a foundation for advancing community sports programs [43]. The observed relationship between cellular mechano-responses and loading patterns suggests the need for diverse activity options to optimize population health [44]. Long-term health improvements require sustained engagement in community sports programs, as evidenced by sequential cellular response patterns [45].

Comprehensive analysis of molecular data supports the implementation of both structured and unstructured activities to accommodate individual preferences and capabilities [46]. Cellular response patterns validate the importance of progressive programming [47], while participation duration and cellular stress resistance metrics emphasize the need for accessible, year-round community facilities [48]. The molecular basis for adaptation through varied movement patterns supports the development of multi-sport facilities and diverse activity programs [49].

5. Conclusions

This research provides comprehensive insights into exercise-induced adaptations among sports town residents, demonstrating significant physiological improvements through a 12-week structured intervention program. The findings reveal substantial enhancements in both cardiovascular fitness (24.2% increase in VO_2 max) and muscular strength (23.5% improvement), supported by molecular evidence of increased AMPK activation (2.8-fold) and enhanced cellular mechanical properties (45.3% increase in elastic modulus). The study establishes clear temporal patterns in adaptation responses, identifying distinct phases that inform optimal program design and implementation. The observed biphasic adaptation pattern, coupled with the integration of molecular signaling pathways and mechanical responses, suggests that effective community exercise programs should incorporate varied activities and loading patterns. The identification of peak pathway activation periods (24–48 h post-exercise) provides practical guidance for program scheduling and progression. These findings advance both theoretical understanding and practical applications in exercise science, offering a scientific foundation for developing evidence-based community exercise programs. The research demonstrates that well-structured sports town facilities and organized exercise programs can effectively promote population health through systematic physical activity engagement, providing valuable guidance for future community health initiatives and sports town development.

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Abbreviations

AMPK	AMP-activated protein kinase
PGC-1α	Peroxisome proliferator-activated receptor gamma coactivator 1-alpha
mTOR	Mammalian target of rapamycin
FAK	Focal adhesion kinase
GLUT4	Glucose transporter type 4
CPT1	Carnitine palmitoyltransfer

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