High-intensity interval training activates telomerase and reduces p53 expression

C. Werner, M. Hauser, K. Schirra, T. Meyer¹, M. Böhm, U. Laufs

Klinik für Innere Medizin III, Kardiologie, Angiologie und Internistische Intensivmedizin, Universitätsklinikum des Saarlandes, Homburg/Saar, Germany

¹Institut für Sport- und Präventivmedizin, Universität des Saarlandes, Saarbrücken, Germany
I have nothing to disclose.
Physical exercise and cardiovascular risk
- Epidemiology -

Women's Health Initiative (prospective observational study)

Cardiovascular Risk

![Graph showing the relationship between metabolic equivalents and cardiovascular risk in white women. The graph indicates a significant trend with P for trend < 0.001.](image)

Metabolic Equivalents

- Quintile of total MET score
- Lowest to Highest

Manson et al., NEJM 2002;347:716-725
Physical exercise increases life expectancy
- Epidemiology -

Prospective cohort study, N=416,175, average follow-up 8 years, exercise questionnaire

15 minutes a day of moderate-intensity exercise may increase life expectancy

Wen et al., Lancet 2011;378:1244-1253
Aging is the main risk factor for cardiovascular disease
Telomeres regulate cellular aging
Telomerase counteracts telomere erosion

- Centromere
- Chromosome
- Telomere
- Telomere Repeat
- T-LOOP
- Shelterin Complex
- TRF1
- TRF2
- Telomerase
Effects of exercise on human telomere biology?
Physical exercise prevents cellular senescence in circulating leukocytes and in the vessel wall

**Young volunteers**
- 32 young athletes
- 26 young controls

**Middle-Aged volunteers**
- 25 master athletes
- 21 aged controls

**Track and field athletes**
*(Deutscher Leichtathletikverb.)*
- Mean age: 20 years
- Disciplines: 1500m - 10000m
- Distance: ~73 km/wk
- Duration: ~14 h/wk
- Watt / kg: 5.2

**Master athletes**
*(Deutscher Sporthbund)*
- Mean age: 51 years
- Disciplines: triathlon, marathon
- Distance: ~80 km/wk
- Duration: ~14 h/wk
- Watt / kg: 3.8

Non-smoking, healthy age- and gender- matched controls without regular exercise

Werner et al., Circulation 2009:120:2438-47
Physical exercise prevents cellular senescence in circulating leukocytes and in the vessel wall

Young volunteers

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Middle-Aged volunteers

- 25 master athletes
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Circulating mononuclear cells

- Assessment of telomere biology
- Analysis of senescence factors

Exclusion criteria: smoking, cardiovascular disease, permanent medication

Werner et al., Circulation 2009:120:2438-47
Physical exercise prevents cellular senescence in circulating leukocytes and in the vessel wall

National Team of track and field: n=32, mean age: 20 years; ~73 km/wk
Non-smoking, healthy age- / gender-matched controls: n=26

Master athletes: n=25, mean age: 51 years; ~80 km/wk, 35 years of training
Non-smoking, healthy age-/ gender-matched controls: n=21

TRF2

p53

Werner et al., Circulation 2009:120:2438-47
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Telomerase Activity MNC
[% young controls]

Telomere Length Lymphocytes
[kbp]

Werner et al., Circulation 2009:120:2438-47
Physical activity mediates acute TRF2 up-regulation in mononuclear cells

Medical students, n=10, mean age 27 years, non-smoking

Healthy volunteers

↓

Single bout of running exercise

↓

Blood samples before, 0h, 6h, 12h, and 24h after running for 1 hour

![Graph showing changes in TRF2 protein expression over time after running exercise](chart.png)
Physical activity mediates acute telomerase activation in mononuclear cells

Medical students, n=10, mean age 27 years, non-smoking

Healthy volunteers

Single bout of running exercise

Blood samples before, 0h, 6h, 12h, and 24h after running for 1 hour
Untrained healthy subjects, 7♀️3♂️, mean age 44 years, VO₂max < 50ml/min/kg

Healthy volunteers ➔ ECG, treadmill test ➔ Pulse-controlled training

3 supervised exercise sessions per week for 3 months

Warm-Up ➔ 4min 80-90% max.HR ➔ Cool-down

3min 65-75% max.HR

Blood samples before and after the last training session
Effects of interval training on physical fitness

Untrained healthy subjects, 7♀ 3♂, mean age 44 years, $\text{VO}_2\text{max} < 50\text{ml/min/kg}$

<table>
<thead>
<tr>
<th>Metric</th>
<th>Baseline</th>
<th>3 months</th>
</tr>
</thead>
<tbody>
<tr>
<td>BMI</td>
<td>24 ± 3 kg/m²</td>
<td>24 ± 3 kg/m²</td>
</tr>
<tr>
<td>Resting HR</td>
<td>80 ± 15 /min</td>
<td>76 ± 11 /min</td>
</tr>
<tr>
<td>Systolic RR</td>
<td>117 ± 7 mmHg</td>
<td>117 ± 8 mmHg</td>
</tr>
<tr>
<td>Diastolic RR</td>
<td>75 ± 6 mmHg</td>
<td>73 ± 6 mmHg</td>
</tr>
<tr>
<td>$\text{VO}_2\text{max}$</td>
<td>37.5 ± 7 ml/min*kg</td>
<td>37.4 ± 8 ml/min*kg</td>
</tr>
<tr>
<td>Vmax</td>
<td>10.6 ± 1.5 km/h</td>
<td>11.8 ± 2.2 km/h</td>
</tr>
</tbody>
</table>
| PWC150            | 6.6 ± 1.4 km/h | 7.4 ± 1.6 km/h | $p=0.03$ $p=0.02$

PWC150: physical working capacity at heart rate 150/min
No direct effects of training on MNC telomerase

Untrained healthy subjects, n=10, mean age 44 years, BMI 24kg/m², VO₂max < 50ml/min/kg
Up-regulation of MNC telomerase activity after 3 months high-intensity interval training

Untrained healthy subjects, n=10, mean age 44 years, BMI 24kg/m², VO₂max < 50ml/min/kg

* p<0.05
Up-regulation of TRF2 expression after 3 months high-intensity interval training

Untrained healthy subjects, n=10, mean age 44 years, BMI 24 kg/m², VO₂max < 50 ml/min/kg
Lower MNC senescence marker expression after 3 months high-intensity interval training

*Untrained healthy subjects, n=10, mean age 44 years, BMI 24kg/m², VO₂max < 50ml/min/kg*

**p<0.01
Summary

- Dose-dependent association of physical activity and life expectancy
- Molecular mechanisms of exercise involve telomerase activation
- A single exercise bout activates telomerase in circulating cells
- High-intensity interval training increases MNC telomerase activity and reduces p53 expression
In planning: **SAusE** study (**Saarländische Ausdauer-Etappe**)

1. **Training phase** (6 Months)
   - Control Group (n=50)
   - Interval Training (n=50)
   - Continuous Running (n=50)
   - Strength/Endurance Exercise (n=50)

2. **Training phase - Cross-over -** (6 Months)
   - Re-Test*
   - Interval Training (Non-Responders To Continuous Training)
   - Continuous Running (Non-Responders To Interval Training)

**6 Months**

**Follow-up**

**Perspective**

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**6 Months**

**Follow-up**

**Perspective**
Heart Rate vs. Running Speed

Heart Rate

Running Speed

Before Training

After Training

Heart Rate

Running Speed

5 km/h 6 km/h 7 km/h 8 km/h 9 km/h