Utilizing Genomics in Exercise Training

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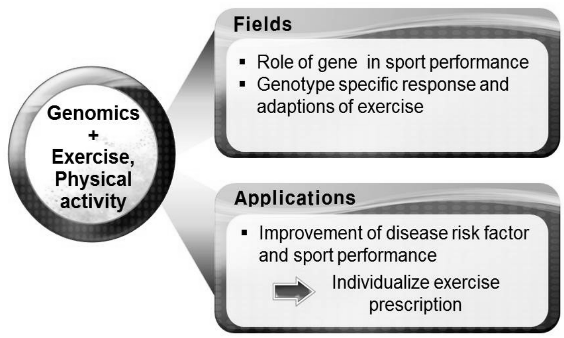
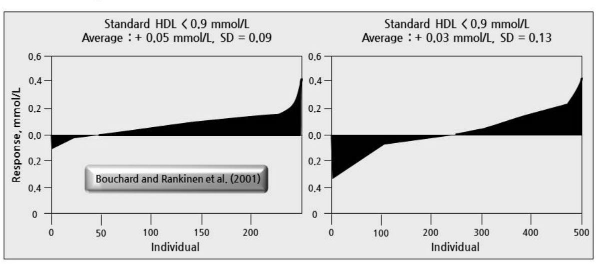
Exercise Genomics?

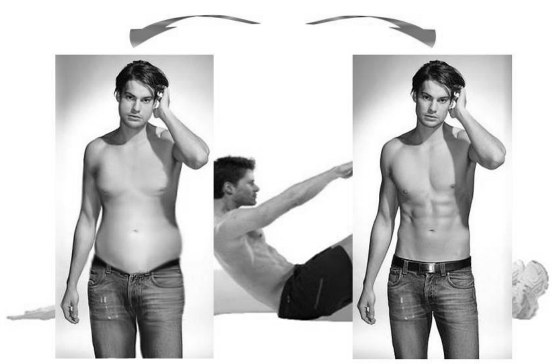


Role of Exercise Genomics

- The results of the study in the field of exercise physiology are reported as the mean
  - Does not explain the diversity of the exercise response and adaptation



Role of Exercise Genomics



Role of Exercise Genomics

- Bouchard et al. (1999) HERITAGE Family Study
  - Individual differences appear largely to changes in VO2max exercise training
  - VO2max is based on an exercise program for 20 weeks seems a very low increase or no change. But It was reported that the average increase 400ml/min
  - Eventually the error that everyone seems to be an increase in VO2max after exercise
- Bouchard & Rankinen(2001)
  - BP, HR, HDL-c changes exhibited by the individual aerobic exercise is a significant difference appears

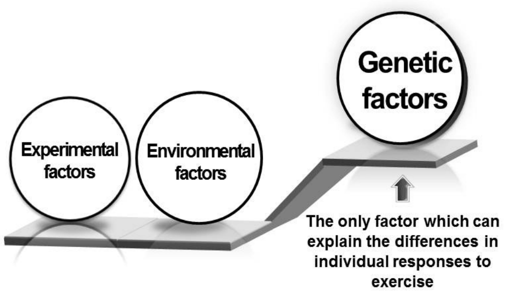
Role of Exercise Genomics

In Conclusion

- **Reaction and adaptation phenomenon caused by the movement of the body**
  - ➡ Appear to vary by individual
  - ➡ It is illogical to the average value representing the result

Role of Exercise Genomics

Three factors for explaining the individual difference



Studies of Exercise Genomics (~ 2005)

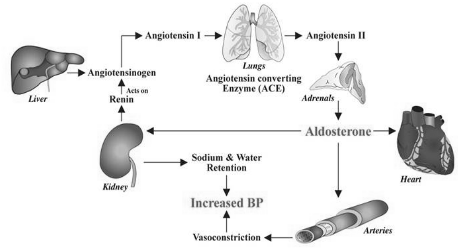
Research results of exercise genomics		
Field	~ 2000 year	2000 ~ 2005 year
Endurance exercise performance and genetic testing	20	53
Muscle strength or anaerobic power	2	23
Blood lipids, inflammatory markers	8	32

ACE gene

Angiotensin-I converting enzyme (ACE) gene

- **One of the most intensely studied gene.**
- **ACE catalyze the conversion of angiotensin I to angiotensin II.**
- **ACE gene is located on chromosome 17q23 and consists of 26 exons and 25 introns.**
- **The insertion deletion (I/D) polymorphism in this gene express to three genotypes, DD, II and ID heterozygotes.**

ACE Gene & Exercise Performance



- **Montgomery (1997)** : DD Genotype, left ventricular hypertrophy↑
- **Montgomery (1998)** : Highlands climber(II Genotype↑)
  - Improve the high shot performance done after exercise training in II genotype

ACE Gene & Exercise Performance

ACE DD & ID Genotype	● Increasing the action of angiotensin II by high activity of the ACE gene increases the burden on the cardiovascular system ⇒ Low aerobic endurance performance
ACE II Genotype	● Low activity of angiotensin II is easy to relax blood vessels and smooth the blood circulation ⇒ High aerobic endurance performance

ACTN3 Gene

- The ACTN3 gene encodes the protein α -actinin-3, which is almost exclusively expressed to sarcomere of the fast glycolytic type II fibers that are responsible for the generation of rapid forceful contractions during activities such as sprinting and weightlifting
- ACTN3 is expressed only in fast twitch fibers
- ACTN3 genotypes : RR, RX, XX

ACTN3 Gene

ACTN3 RR	The α-actinine-3 is expressed in fast twitch fibers
ACTN3 RX	The expression of α-actinin-3 + α-actinin-2
ACTN3 XX	α-actinin-3 (x) → α-actinin-2

ACTN3 Gene & Exercise Performance

ACTN3 RX or XX Genotype

- Fatigue resistance and sustained muscle contraction
- Changes in the form of muscle using the aerobic metabolism
- Effect on aerobic endurance exercise performances

- **Alfred et al. (2011), Chui et al. (2011), Lucia et al. (2006)**
  ⇒ ACTN3 R577X : Associated with aerobic endurance exercise
- **Chan et al. (2011), Chan et al. (2008)**
  ⇒ ACTN3 R577X polymorphism : Determine the type of muscle

Examples of Genotype Specific Exercise Guidelines

INSIG2 genotype & Exercise

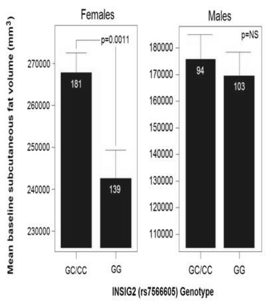
- The INSIG2 promoter SNP rs7566605 (g.-10,1025G>C, chr2:118,552,255, NT_022135.15) was associated with increased BMI
- Functionally linked to lipid metabolism, most notably due to its role in endogenous cholesterol and fatty acid synthesis feedback inhibition
- It is an endoplasmic reticulum membrane bound protein that inhibits the proteolytic activation of sterol response element binding proteins (sreps) in response to cholesterol or insulin
- Animal data suggest a role for insig2 in regulating triglyceride levels in rats

STRENGTH TRAINING		
INSIG2 (rs7566605)		
CC	CG	GG
Less effect		Effect

- Orkunoglu-Suer FE et al. INSIG2 Gene Polymorphism Is Associated With Increased Subcutaneous Fat In Women And Poor Response To Resistance Training In Men. BMC Medical Genetics 9, 117 (2008)

INSIG2 genotype & Exercise

The results of studies



- Women with a copy of the C allele had higher levels of baseline subcutaneous fat but men did not show any such association
- Men homozygous for the G ancestral allele showed a loss of subcutaneous fat, while those with one or two copies of the C allele gained a greater percentage of subcutaneous fat with resistance training

INSIG2 genotype & Exercise

- Exercise Guidelines
  - INSIG2 CG,CC (male) : subcutaneous fat (↑) with resistance training
  - resistance + aerobic exercise (exercise intensity : RER 0.7)
- Exercise Recommendations (for CC,CG)

Mode	Frequency	Duration	Intensity	Progression
Aerobic exercise (walking, stationary bicycle)	4-6 days/wk	20min/session to start	THR 134 -141(40-60% HRR) RPE 13-15/20	Exercise increases the time a week for 5 minutes increasing to 45 minutes. (75-85% HRR)
Resistance Training	3 days/wk	10-15 repetitions	<50% 1 RM	Exercise increases the weight target weight if you can hear comfortably.
Flexibility exercise	3 days/wk	10-20s	Stretch to the point of feeling tightness or slight discomfort.	
Warm up / Cool down		A minimum of 10 mins	RPE 7-9/20	

PPARGC1A genotype & Exercise

The PPARGC1A gene

Coactivator of a subset of genes that control oxidative phosphorylation(termed the OXPHOS genes)

Regulation
- Mitochondrial biogenesis
- Glucose and lipid transportation and oxidation
- Skeletal muscle fiber-type formation

VO2 max

Positively correlated with OXPHOS mRNA levels in human skeletal muscle

OXPHOS gene expression

Coordinately down regulated in diabetic skeletal muscle

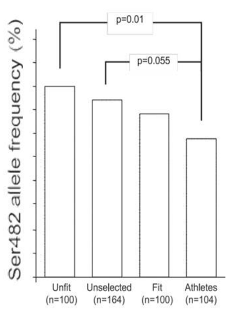
PPARGC1A genotype & Exercise

AEROBIC CAPACITY		
PPARGC1A (rs8192678)		
AA	GA	GG
Decrease	Moderate	

- Saltin B etal. Maximal Oxygen Uptake In Athletes. Journal Of Applied Physiology 23, 353-8 (1967).
- LuciaAetal.PPARGC1AGenotype(Gly482Ser)Predicts Exceptional Endurance CapacityIn European Men. Journal Of Applied Physiology (Bethesda,Md.:1985) 99,344-8 (2005).

PPARGC1A genotype & Exercise

The results of studies



- The frequency of this allele in unfit population controls (40%) is similar to that reported previously in Danish diabetic patients(37%)
- By contrast, fit controls in our study have a lower Ser482 allele frequency (33%), and elite-level athletes have the lowest allele frequency (29%) of all groups

PPARGC1A genotype & Exercise

The results of studies

- A lower frequency of the Ser482 allele is associated with a higher aerobic capacity
- A low level of cardiorespiratory fitness is a strong risk factor for diabetes, it is possible that fitness mediates the previously reported relationship between Gly482Ser genotype and diabetes

PPARGC1A genotype & Exercise

- Exercise Guidelines
  - a Higher frequency of the Ser482 allele : need aerobic exercise to improve cardiorespiratory endurance
- Exercise Recommendations (a Higher frequency of the Ser482 allele)

Frequency	• ≥5 day/wks of moderate exercise, or ≥3 day/wks of vigorous exercise
Intensity	• Moderate and/or vigorous intensity (most adults) • Light-moderate intensity (deconditioned individuals)
Time	• 30-60 min/day of moderate exercise • 20-60 min/day of vigorous exercise
Type	• Walking, leisurely cycling, aqua-aerobics, slow dance
volume	• Increasing pedometer step counts by ≥2,000 steps/day to reach a daily step count ≥7,000 steps/day steps is beneficial

FTO genotype & Exercise

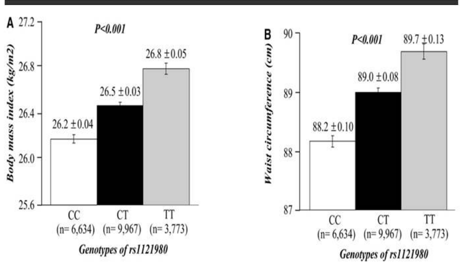
- Human obesity is caused by a complex interplay of genes and environment
- FTO (fat mass and obesity-associated) gene have been found to be robustly associated with obesity-related traits in humans
- FTO gene showed a highly significant association with type 2 diabetes mediated through body mass index (BMI; in kg/m2)

WEIGHT LOSS RESPONSE TO EXERCISE		
FTO (rs1121980)		
TT	CT	CC
Hardly exercise recommendation		Exercise recommendation

- Li S et al. Cumulative Effects And Predictive Value Of Common Obesity-susceptibility Variants Identified By Genome-wide Association Studies. The American Journal Of Clinical Nutrition 91, 184-90 (2010).
- Vimaleswaran KS et al. Physical Activity Attenuates The Body Mass Index-increasing Influence Of Genetic Variation In The FTO Gene. The American Journal Of Clinical Nutrition 90, 425-8 (2009).

FTO genotype & Exercise

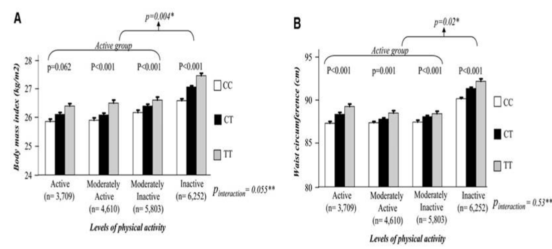
The results of studies



- The risk (T) allele of rs1121980 was significantly associated with BMI (0.31-unit increase per allele; P, 0.001) and WC (0.77-cm increase per allele; P , 0.001)

FTO genotype & Exercise

The results of studies



- Physical Activity attenuates the effect of the FTO rs1121980 genotype on BMI and WC

FTO genotype & Exercise

- Exercise Guidelines
  - obesity induced by FTO variation can be overcome by adopting a physically active lifestyle.
  - TT type : need the combination of moderate reductions in energy intake with adequate levels of physical activity
- Exercise Recommendations (the risk (T) allele of rs1121980)

Frequency	• ≥ 5 day/ wks to maximize caloric expenditure.
Intensity	• Moderate to vigorous intensity aerobic activity should be encouraged. • 40% < 60% VO_2R or HRR → ≥ 60% VO_2R or HRR
Time	• A minimum of 30min/day(i.e., 150 min/wks) progressing to 60min/d(i.e., 300 min/wks) • 30-60 min/day of moderate intensity, aerobic activity.
Type	• Walking, leisurely cycling, aqua-aerobics, slow dance • Swimming, spinning.

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