The 4th International Sport Science Symposium on "Sport Sciences for the Promotion of Active Life"
【Keynote lecture II】

# Introduction to sapiomics and sportsomics

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Sport Sciences, 8, 64-65, 2011
Accepted for publication: 7 March 2011

Recently, I coined two terms, sapiomics and sportsomics. Sapiomics is integrated knowledge about *Homo sapiens* obtained by multi-omic approaches, whereas sportsomics represents multi-omic approaches focusing on sports. At present, targets of various "omics" include the following: the genome, exome, transcriptome, proteome, glycome, metabolome, fluxome, phenome, and diseasome. Because each of these omics is based on huge datasets, integration of multi-omics data requires deep insights into the organisms. Thus, the term sapiomics not only implies that sapiomics' target is *Homo sapiens* but that sapiomics necessitates comprehensive wisdom to understand our own species.

**Beyond the limitations**: There are distinct obstacles in sapiomics and sportsomics because of limited availability of human tissues and cells for these studies. Therefore, we prioritize genomics and exomics for investigation of top world athletes in comparison with elderly citizens or supercentenarians (age ≥ 110). However, we also utilize metabolomics, fluxomics, and phenomics, each of which is useful for characterizing the extreme phenotypes of top athletes as well as supercentenarians.

**Genomics**: We have conducted detailed analysis of the mitochondrial genome of 139 Japanese Olympic athletes (Mikami *et al*. *Br J Sports Med* June 15, 2010*)*. This study is an extension of our studies on the role of mtSNPs (mitochondrial single nucleotide polymorphisms) or mtHAPs (mitochondrial haplogroups) in lonvegity (Bilar *et al*. *PLoS One* 3: e2421, 2008), type-2 diabetes (Fuku *et al*. *Am J Hum Genet* 80: 407–415, 2007), and metabolic syndrome (Tanaka *et al*. *Diabetes* 56:518–521, 2007). We are currently conducting a genome-wide association study (GWAS) on performance-associated single nucleotide polymorphisms (PAPs) by use of Illumina Omni1 or OmniExpress BeadChips. Our preliminary analysis indicates that several genomic regions are associated with the high performance of Jamaican athletes.

**Exomics**: To discover rare variants that contribute to performance in sports, we have started exome analysis. The analysis of all exons (50 mega bases) is quicker and more cost-effective than that of the whole genome (3 giga bases). Another advantage of exome analysis is that the sequence results can be easily interpreted with respect to their effects, such as non-synonymous or non-sense mutations and splice variations. We have finished the exome analysis of 5 Jamaican athletes, 1 Jamaican control, and 4 Japanese athletes. On the other hand, we will soon start exome analysis in search of pathogenic

mutations in 2 patients with mitochondrial respiratory complex I deficiency. Analysis of trio (mother, father, and patient) or quartet (trio plus unaffected sibling) will be useful for identifying pathogenic mutations that are responsible for monogenic diseases. We expect that comparison between the two subject groups, athletes versus patients, will provide us a list of performance-related rare variants. Meanwhile, we have undertaken the exome analysis of the senescence-accelerated mouse (SAM). A total of 10 sub-strains of SAMP1-SAMP11 (senescence-prone) and SAMR1-SAMR2 (senescence-resistant) mice will be surveyed for causative mutations in the protein-coding genes. We expect this study on the SAM exome to shed light on the mechanisms underlying dementia, sarcopenia, and frailty in these mouse models.

**Metabolomics**: We have been analyzing metabolomic changes in 2SD cybrid cells with a mitochondrial DNA mutation (m.3243A>G), when they are exposed to lactate or pyruvate, in collaboration with Prof. Tomoyoshi Soga and Dr. Kenjiro Kami at Tsuruoka Metabolomics Campus of Keio University. The energy charge, ([ATP] + 1/2 [ADP])/([ATP] + [ADP] + [AMP]), of the 2SD cells was decreased by the addition of 10 mM lactate. We also found that lactate increased the levels of methylglyoxal ($CH_3$-CO-CHO) in the 2SD cells. These changes were prevented by the addition of 10 mM pyruvate to the 2SD cells. Methylglyoxal arises from non-enzymatic phosphate elimination from glyceraldehyde 3-phosphate (GAP) and dihydroxyacetone phosphate (DHAP). Methylglyoxal is cytotoxic and is involved in the formation of advanced glycation endproducts (AGEs), which causes atherosclerosis associated with aging. Thus, pyruvate will be effective in maintaining the intracellular energy level, in preventing atherosclerosis, and in promoting longevity, as was demonstrated recently in *C. elegans* (Mouchiroud *et al*. *Aging Cell* 10: 39–54, 2011).

**Fluxomics**: When we administer respiratory substrates labeled with non-radioactive and stable isotope $^{13}C$, we can trace the flux of metabolic intermediates in the body non-invasively (Wu *et al*. *Ann NY Acad Sci* 1201: 111–120, 2010). We are currently analyzing the $^{13}CO_2$ in the expired gas after administration of [1-$^{13}$C]pyruvate, [1-$^{13}$C]acetate or [1-$^{13}$C]leucine to monitor the mitochondrial function of the whole body in athletes and aged subjects with or without type-2 diabetes or sarcopenia.

**Phenomics**: We have started collaboration with Alpha Corporation (Kobe, Japan), which has developed an automated real-time system for recognizing the motion of skeletons and skeletal muscles. We have developed an automated system for measuring gait speed and stride as well as the toe and heel positions by use of an infrared time-of-flight (TOF) imaging system (D-Imager). This camera can be also used for monitoring the indoor activity of elderly subjects; and with it the position of the head and the center of gravity of each individual can be recorded for a month. Non-invasive methods for monitoring physical activity and behavior will be useful for life-space assessment of the elderly.

**Conclusion**: Various approaches based on multi-omics technologies will pave the way to sapiomoics for *Homo sapiens* and sportsomics for *Homo "sportis*."