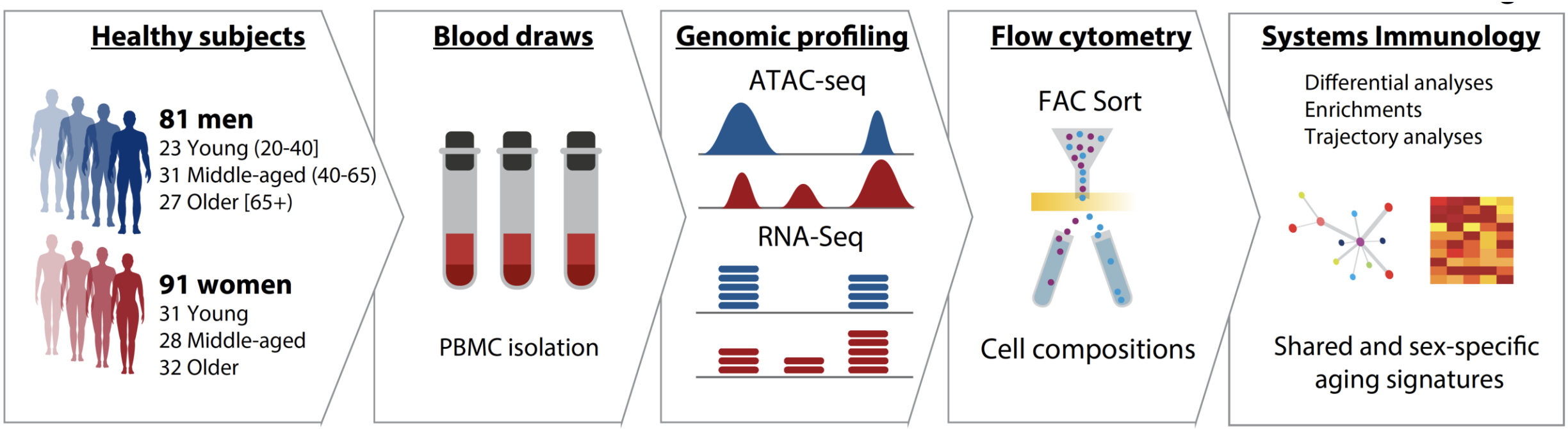
Sex as a Biological Variable in Human Aging Research

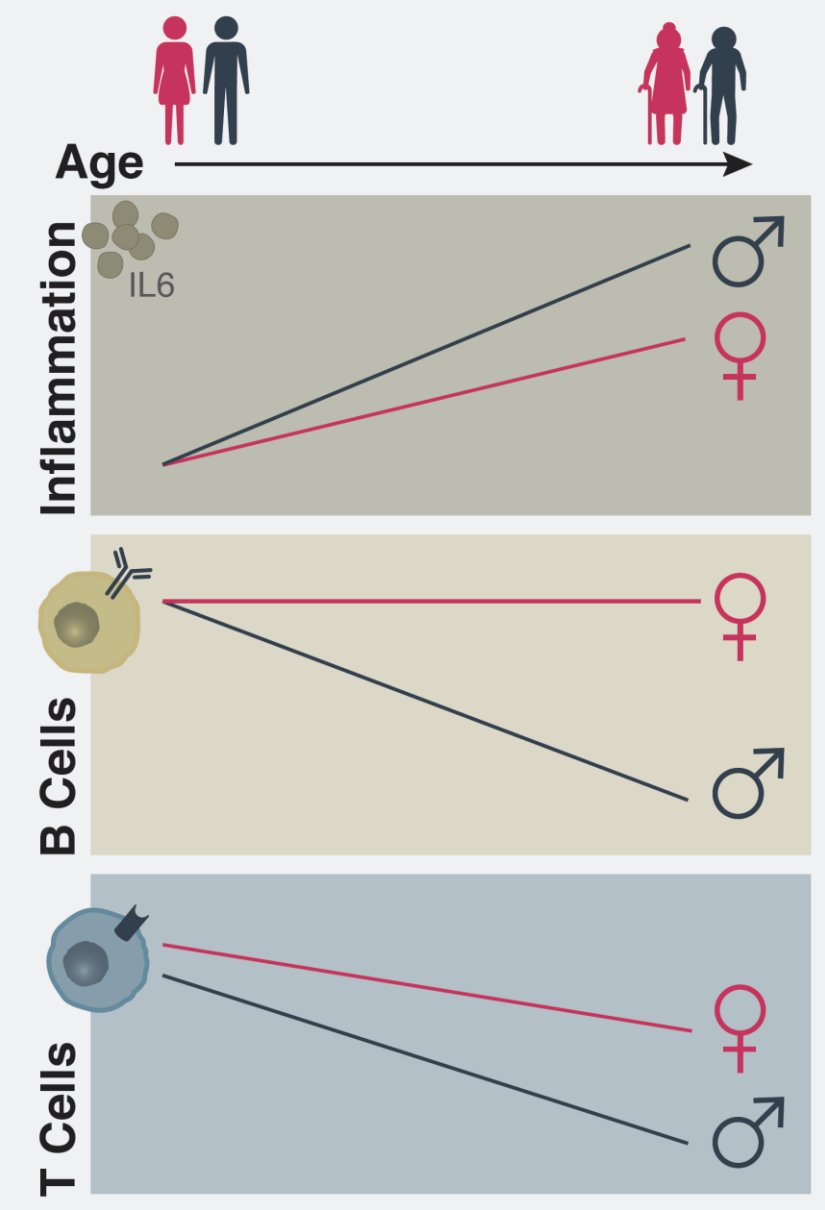
Duygu Ucar, PhD
Associate Professor
Jackson Laboratory for Genomic Medicine
NSC3 Webinar

Careful recruitment of human cohorts to study sex differences in aging



- **Male and female subjects are age-matched and do not differ significantly in clinical parameters (frailty, BMI).**

Major sex differences exist for the hallmarks of immune aging



- Accelerated immune aging phenotype in men
  - Further activation of innate immunity (more inflammaging)
  - Further inactivation of adaptive immunity
  - Earlier start of changes (~5 year)

- Male and female blood immune cells diverge after 65
  - Older women have more active adaptive immunity
  - Older men have more active innate immunity

What are the implications for health and lifespan?

Marquez, …, Ucar
Sexual-dimorphism in human immune system aging
Nature Communications 11: 751, 2020

Sex dimorphism in healthspan and lifespan

- Differences in life expectancy in US
  - For men 76.1 years
  - For women 81.1 years
- Sex dimorphism in immune diseases
  - Susceptibility to infectious diseases and disease severity is higher in men
    - COVID-19 death rate is 1.5 to 2-fold higher for men compared to women
  - Susceptibility to autoimmune diseases is higher in women
    - 90% of lupus patients are women.
- Sex dimorphism in immune responses
  - **How about vaccine responses?**