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Integrative approach to understand early-onset clear cell renal cell carcinoma in racially/ethnically diverse patient populations

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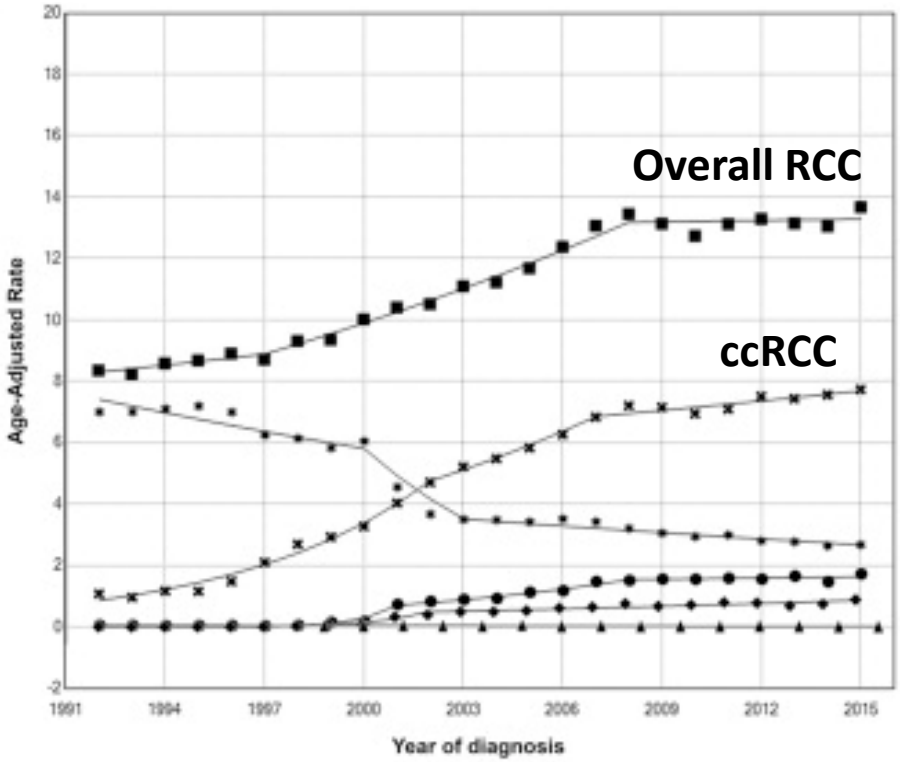
Kidney Cancer Research Summit (Sept 12-13, 2019)

Background

- Kidney cancer incidence rate increased from 1980 to 2010, especially in
  - Younger age group (age<50)
  - Young Native Americans (age 20-49)
- Incidence rate of clear cell renal cell carcinoma (ccRCC) continues to increase.
- Coincide with increase in obesity rates, especially in
  - Younger generations
  - Racial/ethnic minority groups (Native Americans, Hispanic Americans, and African Americans)
  - Obesity - risk factor - ccRCC

RCC incidence rates by histological subtypes



From Saad et al. 2019

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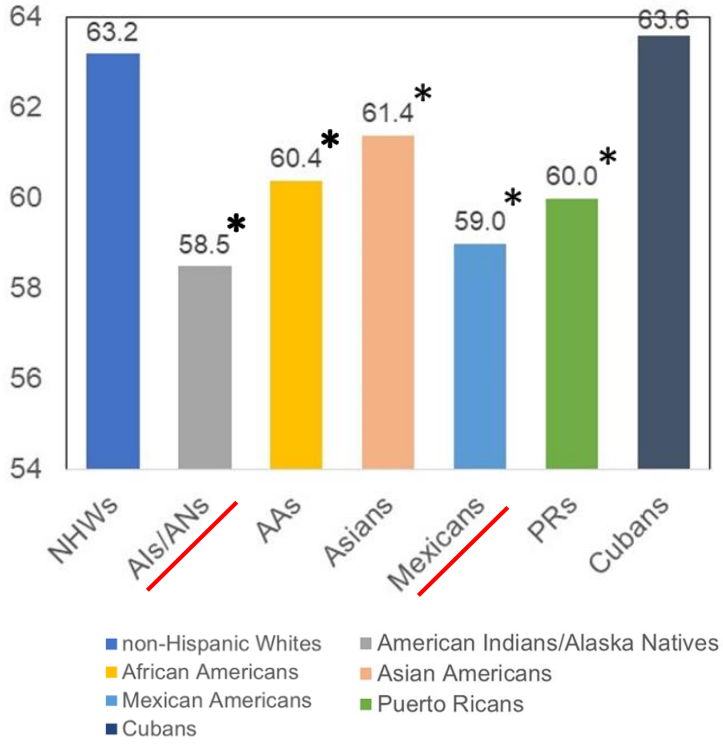
Research Questions

- Research Questions
  - What is the biologic mechanism of early-onset ccRCC?
  - What are risk factors of early-onset ccRCC?
  - How obesity affect early-onset?
- Focus on populations with a heavy burden of RCC
  - Native Americans – 2-fold increased kidney cancer mortality rate
  - Hispanic Americans – 40-50% increased mortality rate
  - They are diagnosis at a younger age.
  - ccRCC is more common among them than European Americans.
  - Race/ethnicity and obesity were independently associated with a young age of diagnosis.
- Arizona is uniquely situated.

Age at diagnosis (NCDB)



Batai et al. 2019 Clinical Genitourinary Cancer
Batai et al accepted to Cancer Medicine

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Current Project (Pilot)

- Hypothesis

  Racial/ethnic minority groups with a heavy burden of RCC have previously uncharacterized or not-well characterized molecular signatures of early-onset and aggressive ccRCC.

- Molecular characterization of early-onset and aggressive ccRCC
  - Screening of germline and somatic *VHL* mutations
    - ✓ Characteristics of patients with and without *VHL* mutations
    - ✓ Not all early-onset patients have germline and somatic mutations (n=77)
  - Whole transcriptome sequencing (TempO-Seq)
    - ✓ Gene expression signatures associated with early-onset and aggressive ccRCC
    - ✓ *PPP1R1A*, a subunit of PP1 (Protein phosphatase 1) is overexpressed in early-onset ccRCC
      - highly expressed in the kidney, liver, and fat
      - PP1 is involved in glycogen metabolism

Supported by
- Urology Care Foundation Research Scholar Award
- University of Arizona Cancer Center Support Grant

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Future Projects

- Research goals
  - Better characterization of early-onset ccRCC
  - Better understanding of roles of obesity or adiposity in earl-onset ccRCC
- Multi-omics approach
  - Whole transcriptome sequencing
  - Whole exome sequencing
  - Epigenomic profiling
  - Metabolomic profiling
- Intra-tumor heterogeneity – spatial profiling
- Racial/ethnic minority groups

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Thank you!

Comments and Suggestion?