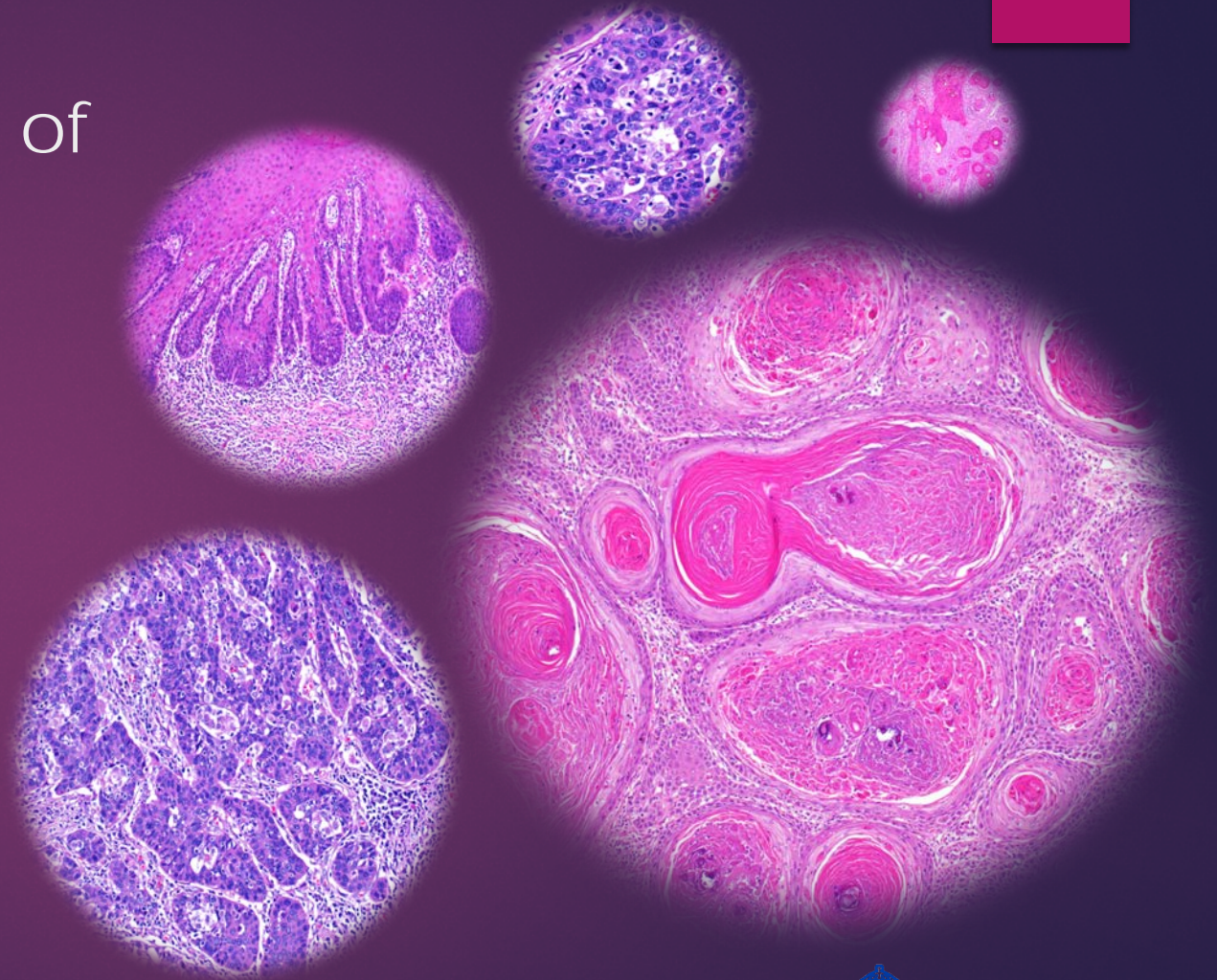


Clinicopathologic Features of Human Papillomavirus Dependent and Independent Vulvar Squamous Cell Carcinoma

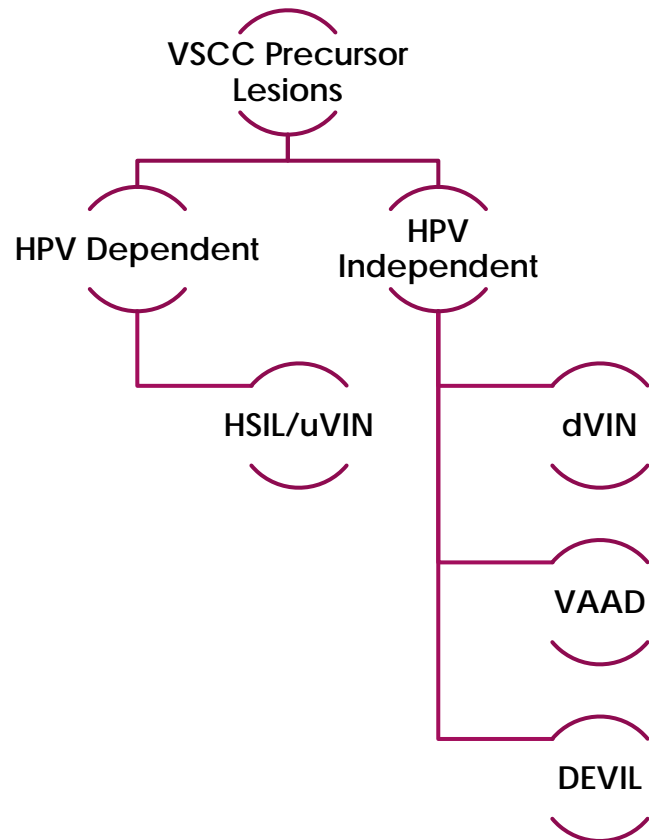
MICHAELA KOP

PI: KOAH VIERKOETTER, MD

2021 QUEEN'S SUMMER RESEARCH INTERNSHIP

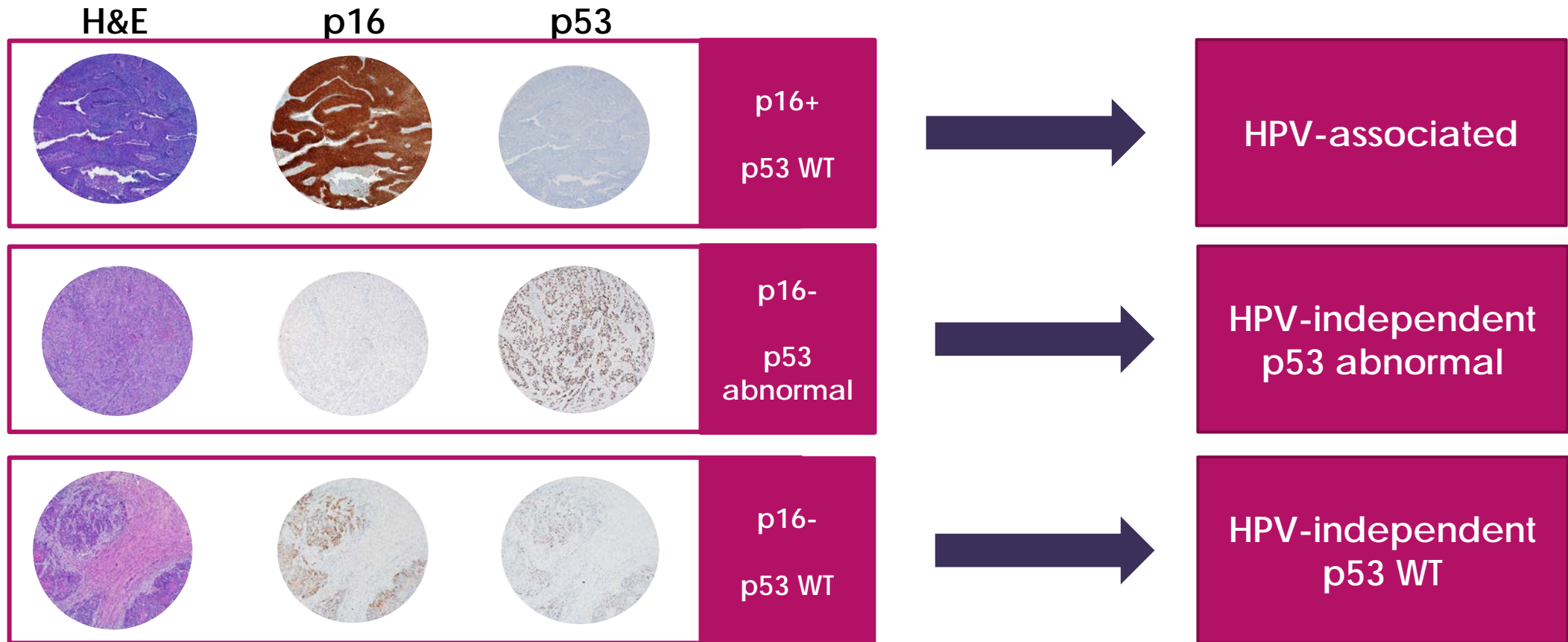


Vulvar Squamous Cell Carcinoma Overview



- ▶ Vulvar squamous cell carcinoma (VSCC) can arise in through two distinct pathways:
 - ▶ HPV-dependent pathway
 - ▶ HPV-independent pathway
- ▶ VSCC is preceded by precursor lesions associated the HPV-dependent and HPV-independent pathways
- ▶ HOWEVER, it is difficult to determine HPV status based on morphology alone
- ▶ Immunohistochemical staining:
 - ▶ p16 can act as a surrogate marker for HPV
 - ▶ Some precursor lesions are both p16- **and** p53 WT (VAAD and DEVIL)

VSCC Histology



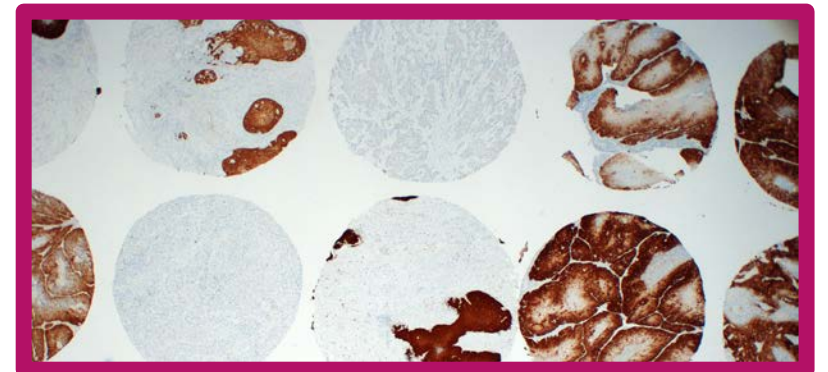
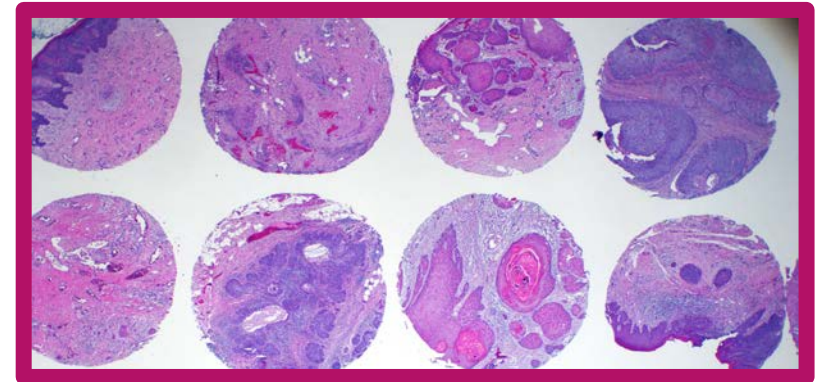
Rates of VSCC Based on HPV Status

Study	Percent HPV-related
Allo et al. (2019) n=144; Canada	32% HPV-related
Hinten et al. (2018) n=318; Netherlands	17% HPV-related
McAlpine et al. (2017) n=197; Canada	40% HPV-related
Wakeham et al. (2017) n=62; United Kingdom	52% HPV-related
Lee et al. (2016) n=57; United States	27% HPV-related
Alonso et al. (2011) n=98; Spain	19% HPV-related
Pinto et al. (2004) n=161; Brazil	23% HPV-related

- ▶ Incidence of HPV-related VSCC varies depending on location of study (Rakislova, 2017)
- ▶ HPV-positivity ranges from 18% - 75% (Rakislova, 2017)
- ▶ No previous investigation of VSCC in Hawaii
- ▶ **Thus, this study will yield data applicable to the diagnoses and treatment of Hawaii's diverse population.**

Methods

- ▶ VSCC cases from 1995 – 2020 identified through a search of pathology database (CoPath)
- ▶ Tissue microarray (TMA) constructed by the University of Hawaii Cancer Center (UHCC) and subjected to P16 and P53 immunohistochemical (IHC) staining to determine HPV status
- ▶ IHC stains read by experienced gynecological pathologists, Dr. Koah Vierkoetter and Dr. David Shimizu
- ▶ Patient chart review conducted through a search of the EMR (CareLink)



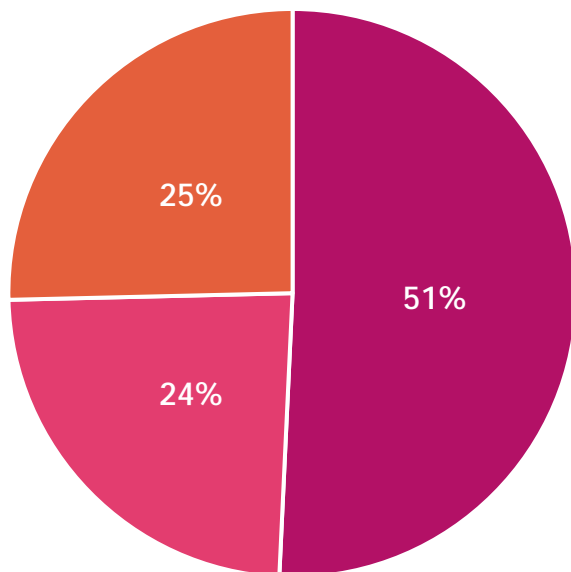
Demographics

Table 1. Demographics

n=67		Pathologic parameters	
Clinical parameters			
Age (years)	69 (Range 33-93)	HPV status (p16 stain)	
Ethnicity (self-reported) (n=43)	White/Caucasian	HPV related	34
	Asian	HPV independent	33
	Native Hawaiian/Pacific Islander	Tumor size	
	Hispanic	< 2.0 cm	20
	Unknown	≥ 2.0 cm	44
BMI (n=42)	Underweight (<18.5)	Depth of invasion	
	Normal (18.5 - 25.0)	≤1.0 mm	7
	Overweight/obese (>25.0)	>1.0 mm	54
	Unknown	Stage	
Smoking history (n=44)	Yes	IA	9
	No	IB	40
	Unknown	II	6
		III	12

HPV-related VSCC Incidence

VSCC Subtype Incidence in Hawaii



■ p16 + p53 WT ■ p16 - p53 abnormal ■ p16 - p53 WT

Table 2. Immunohistochemical results

	P53 status		
	p53 abnormal	p53 WT	Total
p16 + (HPV-related)	0	34	34
p16 - (HPV-independent)	16	17	33

Factors Associated With HPV Status

Table 3. Factors associated with HPV associated and independent status

	HPV associated (n=34)	HPV independent (n=33)	p value*
Age	62.79 (SD 15.42)	75.39 (SD 13.74)	0.0008
Smoking history (n=44)			
Yes (n=27)	15	12	0.1244
No (n=17)	5	12	
BMI (n=42)			
Not overweight/obese (≤ 25.0)	8	11	0.7634
Overweight/obese (> 25.0)	11	12	
Tumor size (n=64)			
< 2.0 cm (n=20)	14	6	0.0577
≥ 2.0 cm (n=44)	18	26	
Depth of invasion (n=61)			
≤ 1.0 mm (n=7)	6	1	0.1064
> 1.0 mm (n=54)	26	28	
Stage			
I (n=49)	28	21	0.1036
II-III (n=18)	6	12	

*p-value less than 0.05 (≤ 0.05) is considered statistically significant

Change in HPV-associated Cases Over Time

Changes in HPV-associated Cases Over Time

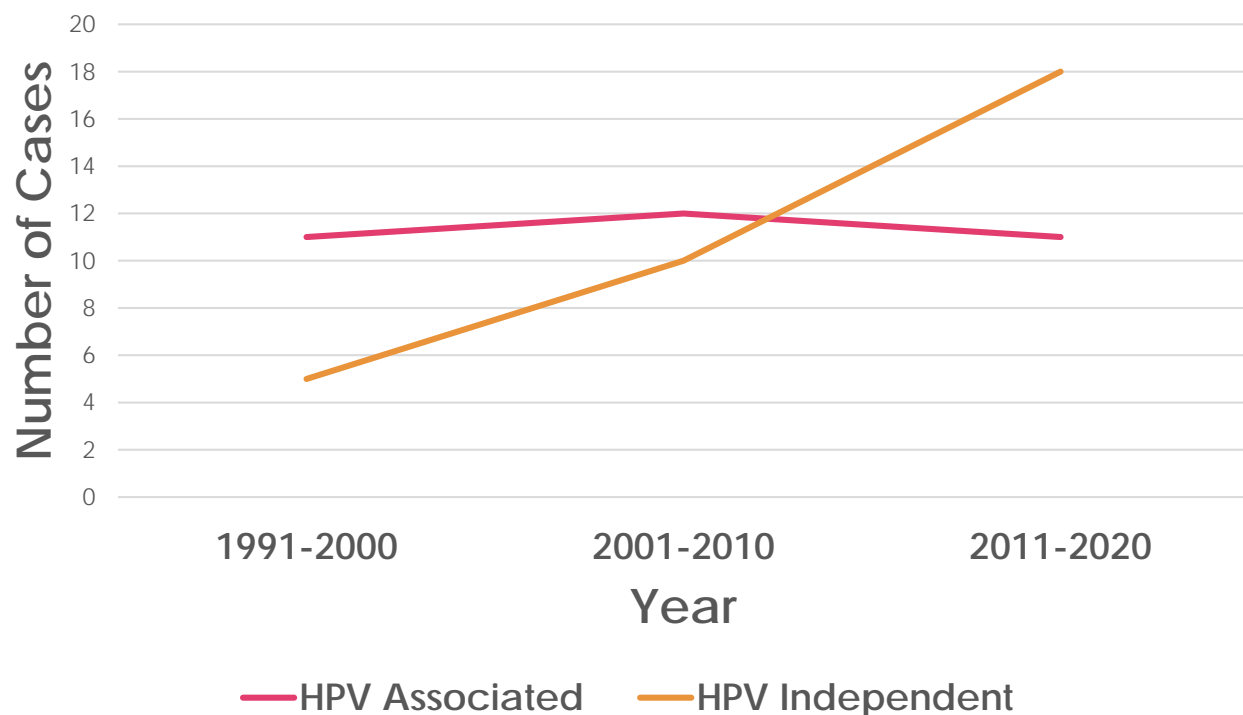


Table 4. Change in HPV-associated cases over time

	HPV Associated	HPV Independent
1991-2000	11	5
2001-2010	12	10
2011-2020	11	18

Discussion & Conclusions

- ▶ Younger average age for HPV-associated VSCC(63 yrs) and higher average age for HPV-independent VSCC (75 yrs)
 - ▶ Agrees with literature – HPV-independent VSCC affects older women while HPV-related VSCC affects relatively younger women (Weinberg, 2019)
- ▶ 51% of VSCC cases in Hawaii are HPV-related
- ▶ 25% of VSCC cases in Hawaii are HPV-independent and P53 WT

Acknowledgements

- ▶ Research Participants
- ▶ Primary Investigator – Dr. Koah Vierkoetter
- ▶ Coinvestigators – Dr. David Shimizu & Dr. Keith Terada
- ▶ Queen's Medical Center Pathology Department
- ▶ University of Hawaii Cancer Center
- ▶ Queen's Medical Center Summer Research Internship
- ▶ Other Collaborators – Dr. Asia Ayabe & Dr. Mayumi Fernandez

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