Oral Cancer

Yuniardini S Wimardhani, Febrina R Prianto
Department of Oral Medicine
Faculty of Dentistry
University of Indonesia

I. Epidemiology, pathogenesis, diagnosis and screening

II. Molecular biology research: clinical usefulness and applications

[1]Epidemiology

- Oral cancers: all cancers in lips, tongue and oral cavity. (ICD-10)
- Histologically >90% of are Squamous Cell Carcinoma (OSCC).
- 11th most common cancer
- OSCC: an important health problem: >274.000 new cases/year, mostly in: India and South East Asia. Mostly in late stage. (Parkin, 2002)

[2]Epidemiology

- Mortality:20 to 40 per 100.000 in Central and Western Europe. (Dobrossy, 2005)
- Despite treatment, only half of patients survive 5 year after diagnosis.
- Prognosis improved with early diagnosis.

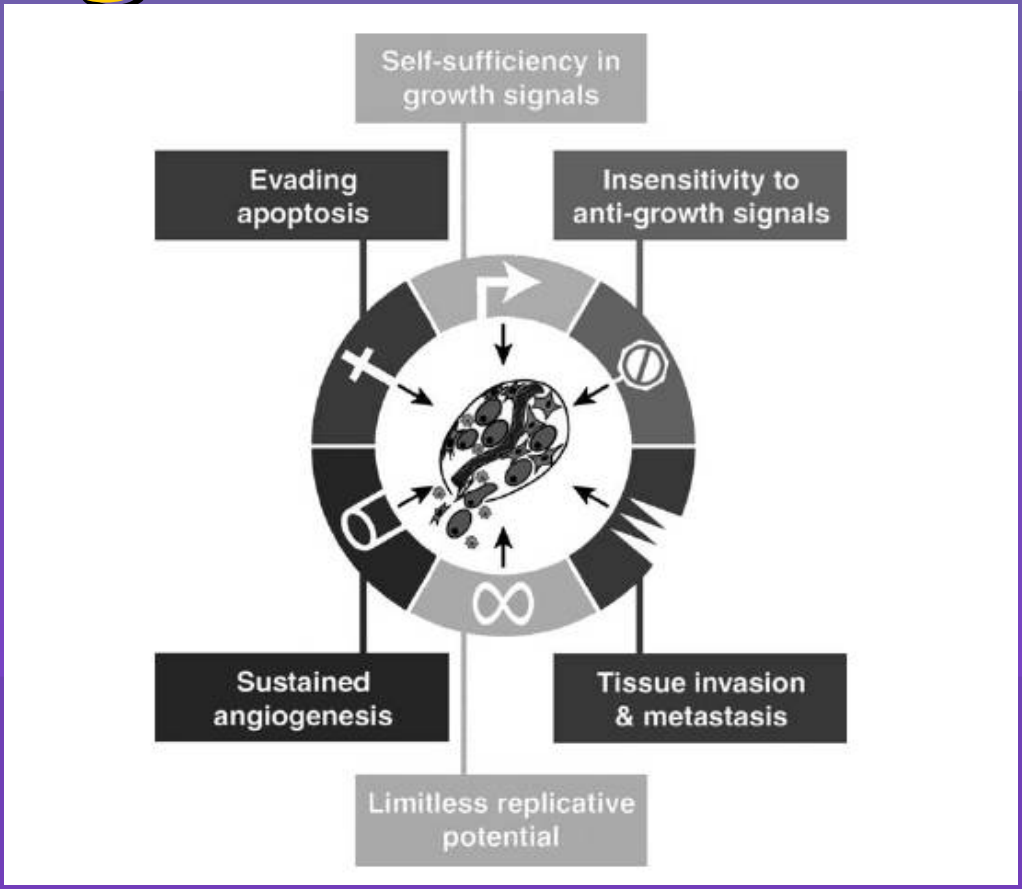
[1]Pathogenesis

- Causal: Multifactors, a combination of extrinsic and intrinsic factors in a period of time

Known risk factors:

- Alcohol
- Tobacco consumption (smoked, chewed, snuffed)
- Betel quid
- Others: UV light, dietary factors, viruses
- Indications: family history or genetic susceptibility

[2]Pathogenesis



(From Hanahan D, Weinberg RA. The hallmarks of cancer. Cell 2000;100(1):57–70)

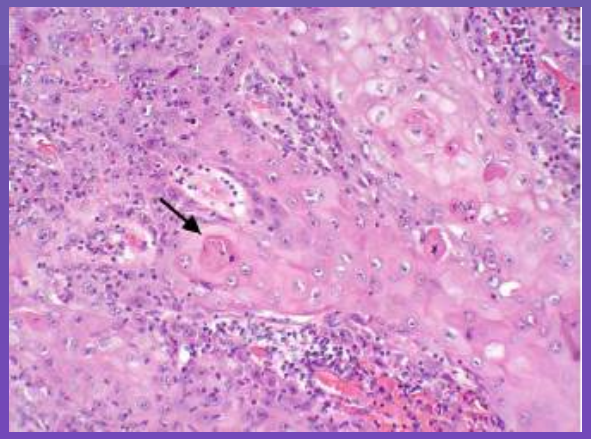
Diagnosis- Clinical

- Early stage as a symptomatic or asymptomatic superficial white lesion, red lesion presented as an ulcer.
- Often progress into a symptomatic or asymptomatic exophytic nodule or tumor with an eroded/ulcerated surface, firm→ non-movable mass.

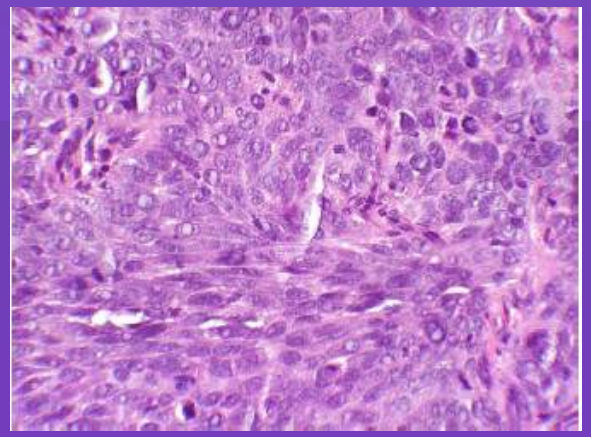
From Kupferman, 2006

Diagnosis-Histophathology

- Biopsy incision/excision
- Loss of part of basement membrane integration.
- Extends to lamina propria as broad sheets, nests, cords, and islands neoplastic cells of epithelial origin.
- Well differentiated
- Moderately differentiated
- Poorly differentiated



Well differentiated



Poorly differentiated

Screening

- For suspicious lesions and amongst high risk population

- Direct visualization
- Toluidine Blue
- Exfoliative cytology and Oral CDx
- DNA ploidy
- Laser-induced fluorescence

Molecular biology research in oral cancer

- Carcinogenesis
- Pathogenesis
- Diagnosis
- Treatment
- Prognosis

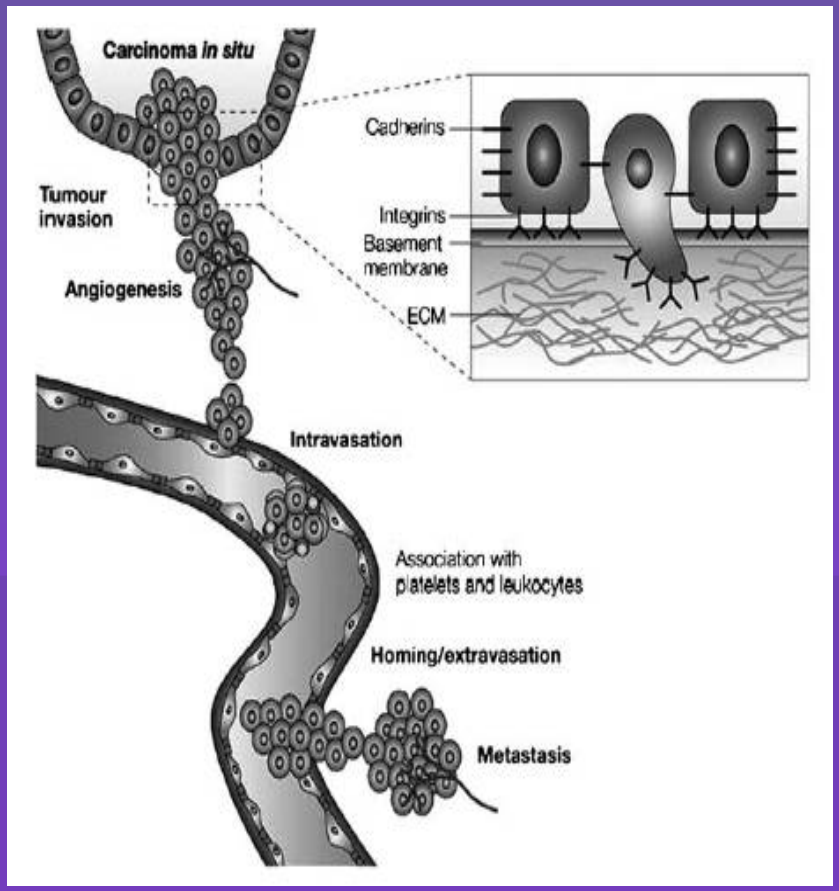
Carcinogenesis

Cancer-controlling genes: :

Gene	Chromosome	Protein and ligands	Function	Expression	Frequency
(Proto)-Oncogenes					
erb-B1	7p13-q22	EFGR, TGF-alpha	Growth factor, growth factor receptor	Overexpression	>30%
c-Myc		c-Myc	Cell growth, apoptosis	Amplification, overexpression	20-40%
H-ras	17p	p21	Mitogenic signalling	Amplification	30-40%
PRAD-1	11q13	Cyclin D1	Cell cycle regulation	Amplification	30-50%
hst-1/int-2	11q13	protein homologue to FGF	Angiogenic activity, growth signalling	Amplification	30%
Stat-3		STAT protein	Cytokine signalling, cell proliferation	Activation, overexpression	80%
Tumour Suppressor Genes					
p53 gene	17p13.1	p53	Cell cycle regulation, DNA repair, cellular differentiation, apoptosis	Overexpression	50-60%
p16	9p21	Cyclin Dependent Kinase p16	Cell cycle progression	Loss of expression	63%-80%
pRb		Cyclin Dependent Kinase p16	Cell cycle progression	Loss of expression	66%

Pathogenesis

- Independent growth signals
- Not sensitive to growth inhibitor signals
- Passing apoptosis
- Unlimited cell cylcle
- Angiogenesis
- Invasion and metastasis



(From Guo W, Giancotti FG. Integrin signaling during tumor progression. Nat Rev Mol Cell Biol 2004;5(10):816–26)

Diagnosis

Saliva-based test

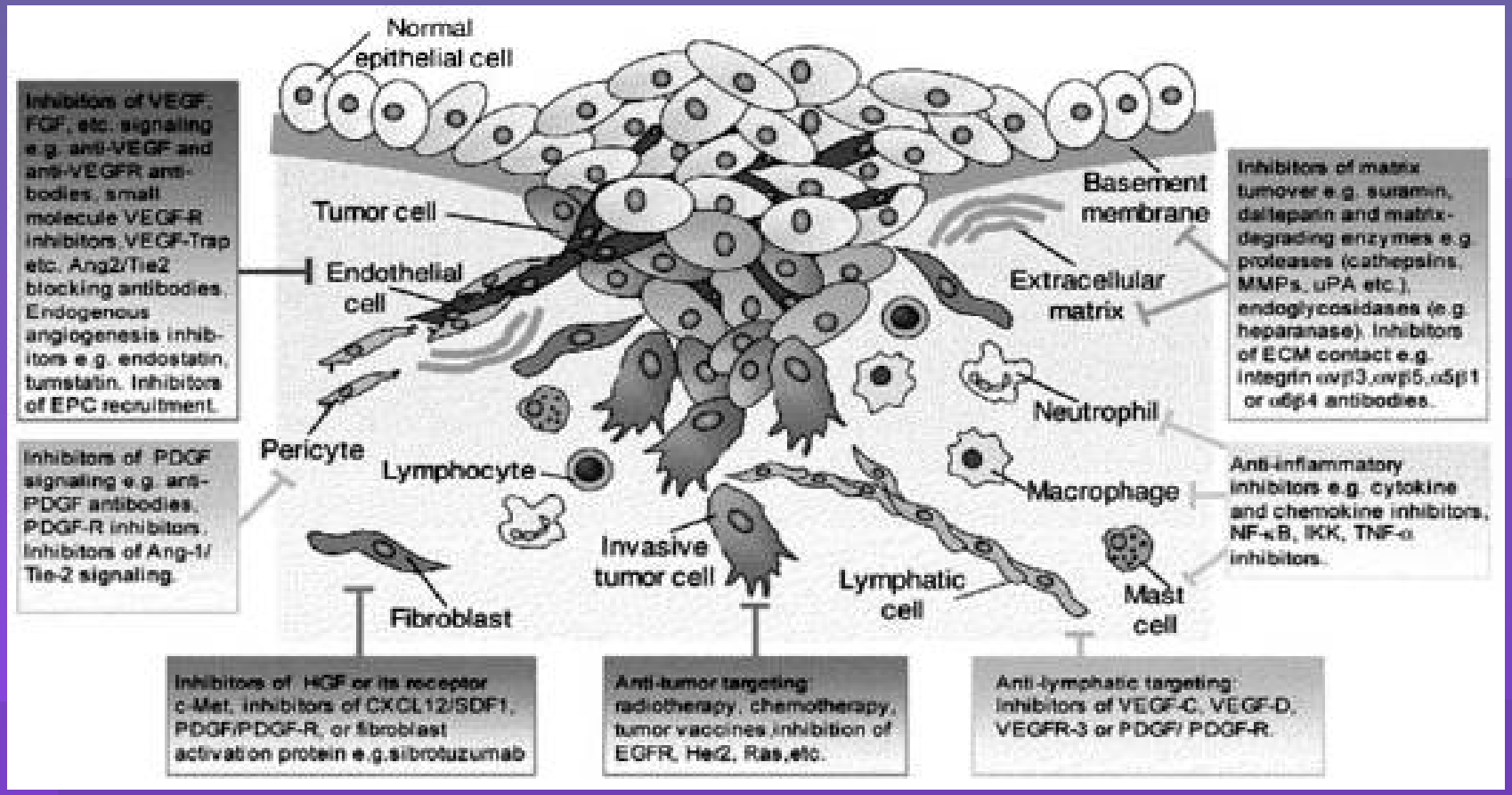
- Epidermal Growth Factor (Balicki, 2004)
- Telomerase activity (Zhong, 2005)
- Gene expression profiling using DNA microarray (Li, 2004, Westra, 2004)

Treatment

- Understanding carcinogenesis in OCSCC → the development of therapeutic strategies dysregulating tumour environment (Joyce, 2005)

Clinical trials

- angiogenesis inhibitors
- growth factor receptor tyrosine kinase inhibitors
- cell cycle regulators



(From Joyce JA. Therapeutic targeting of the tumor microenvironment. Cancer Cell 2005;7(6):513–20)

Summary

- Advances in understanding carcinogenesis in OCSCC develop therapeutic strategies targeting agents that regulate tumour environment.

- Understanding the carcinogenesis would facilitate treatment of patients since many future therapies will be based on this complex cellular mechanism

Any Questions and comments??

Contact:

Yuniardini S Wimardhani

yswimardhani@yahoo.com

Thank You