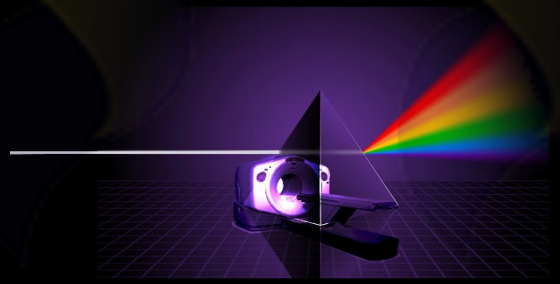
5TH ANNUAL Miami Thyroid Oncology Symposium

March 18-19 2022



Physiologic and Molecular Basis of RAI Theranostics

Seza Gulec

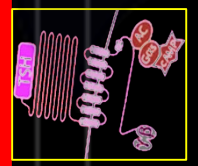
March 18, 2022

RAI Theranostic Circuit

SLC5A5

SLC26A4

SLC5A8



IYD/DEHAL1

T1
T2

TPO

DUOX1

DUOX2

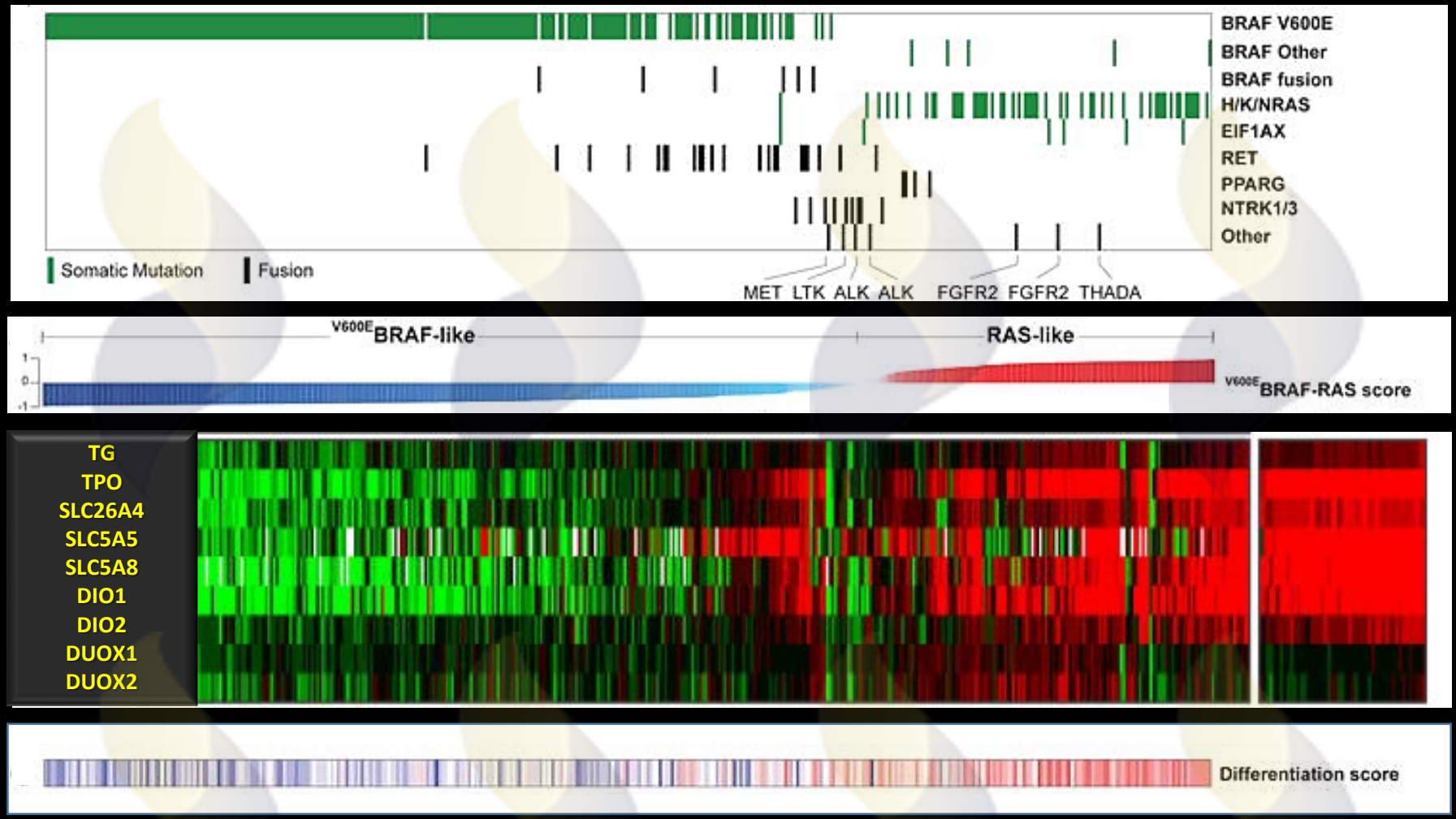
SLC16A2

T3/T4

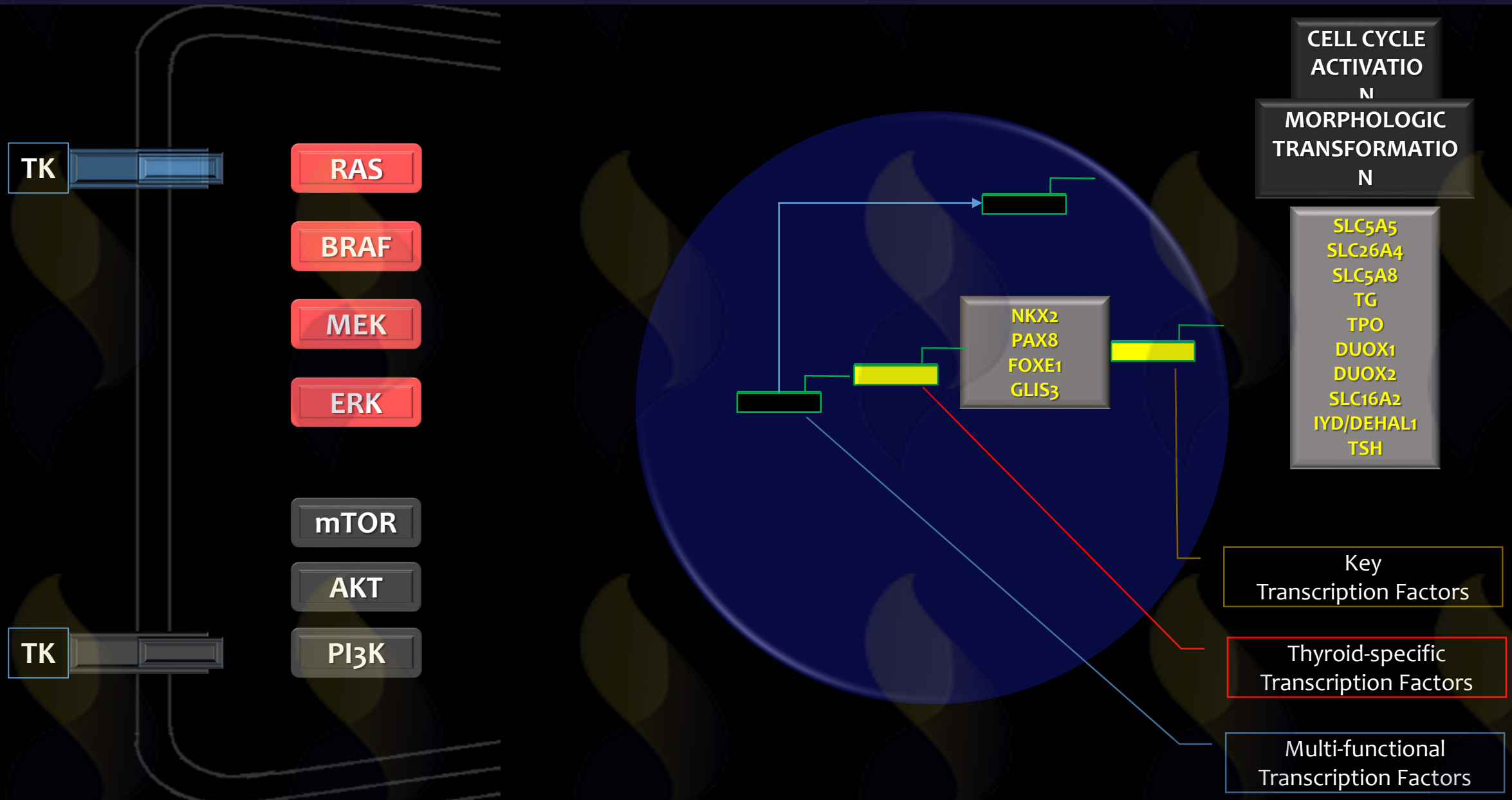
T1/T2
T3/T4

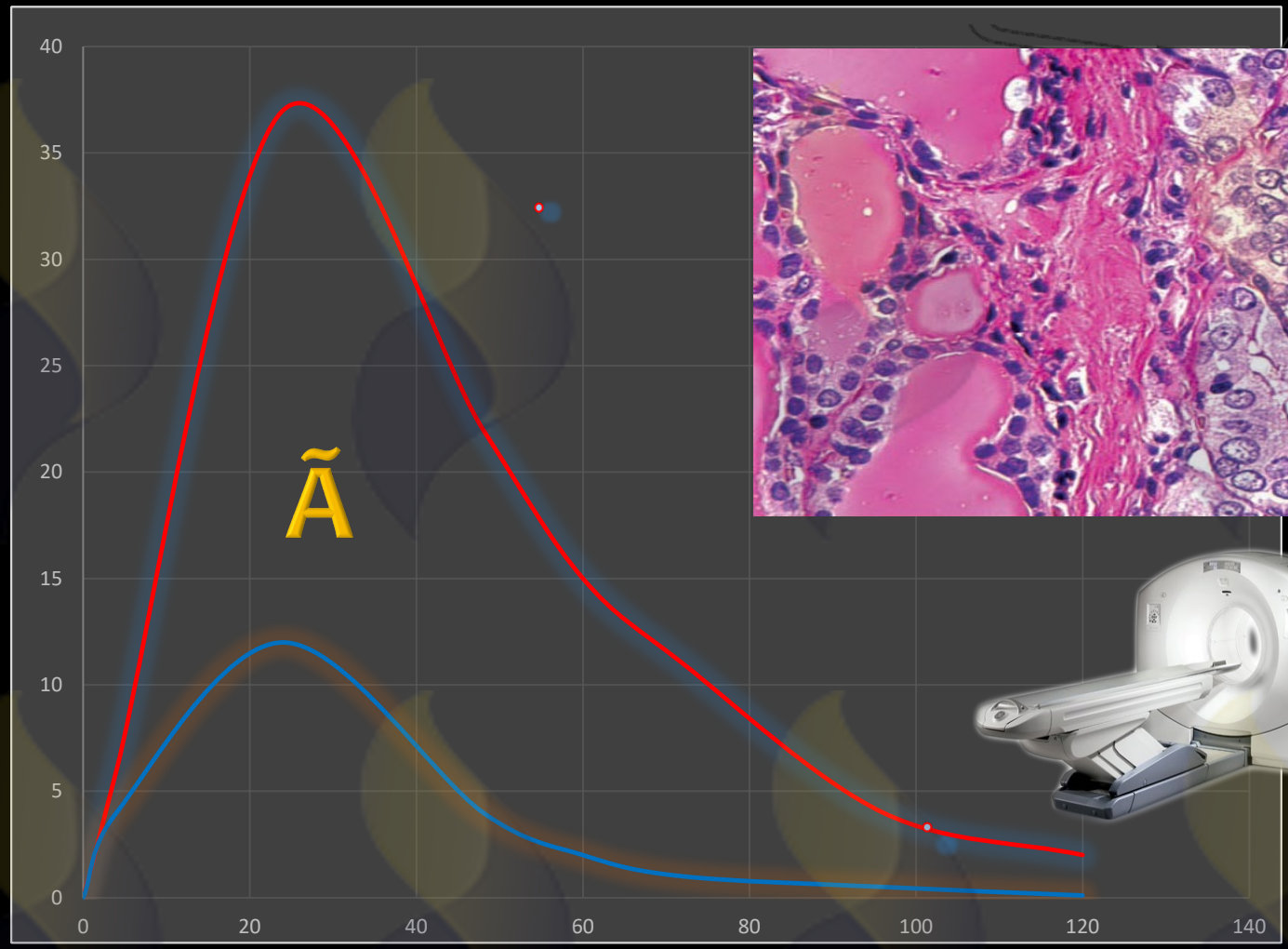
sezaG

Oncobiology: Genomics and Transcriptomics



Oncobiology: MAPK Pathway Activation and ERK Output

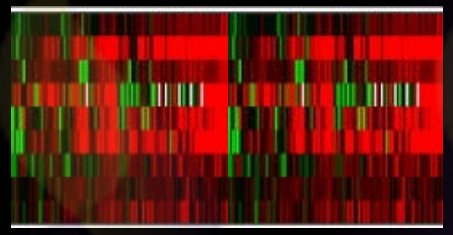




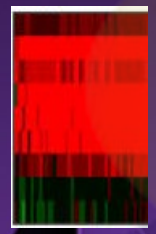
Theranostic Power & Cumulated Activity

Theranostic/Therapeutic Performance of RAI

TDS
ERK Output Modulation

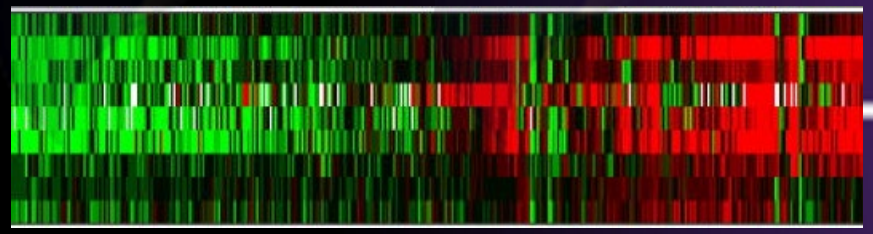


TDS
Normal thyroid
100%



Theranostic Power

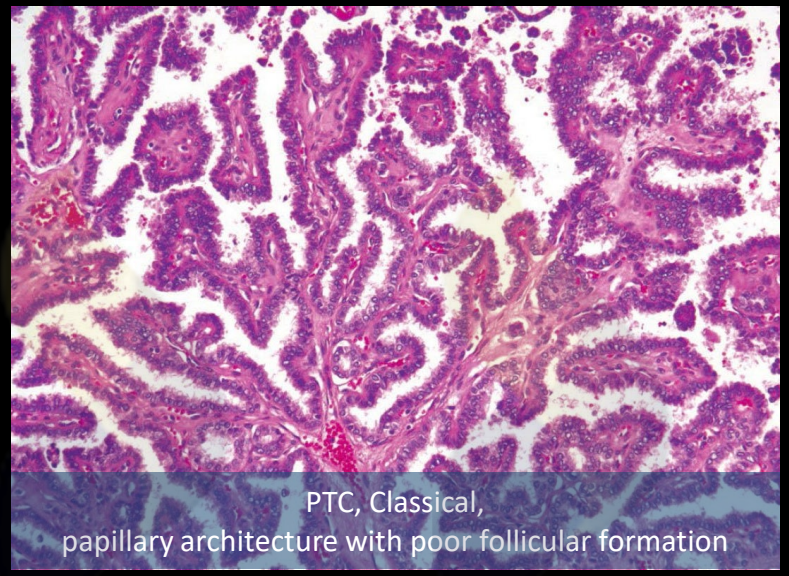
Theranostic Performance



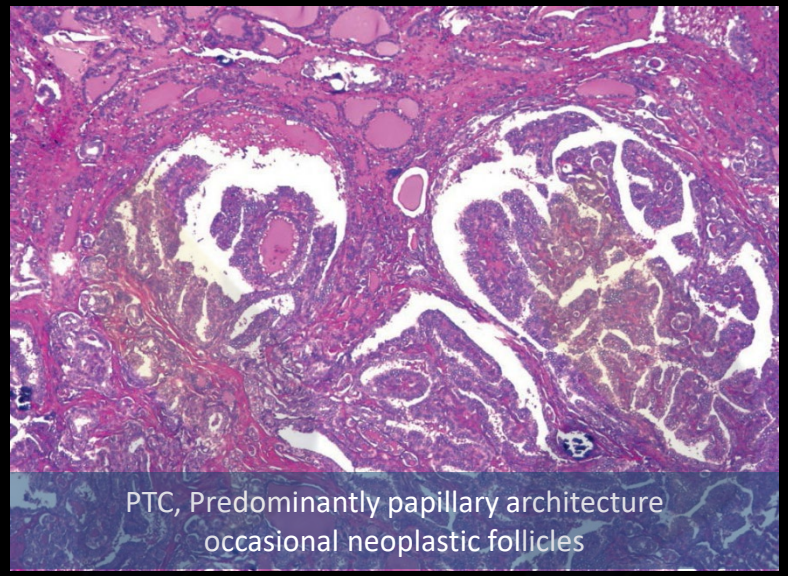
TDS
Papillary Thyroid Cancer

Theranostic Technique

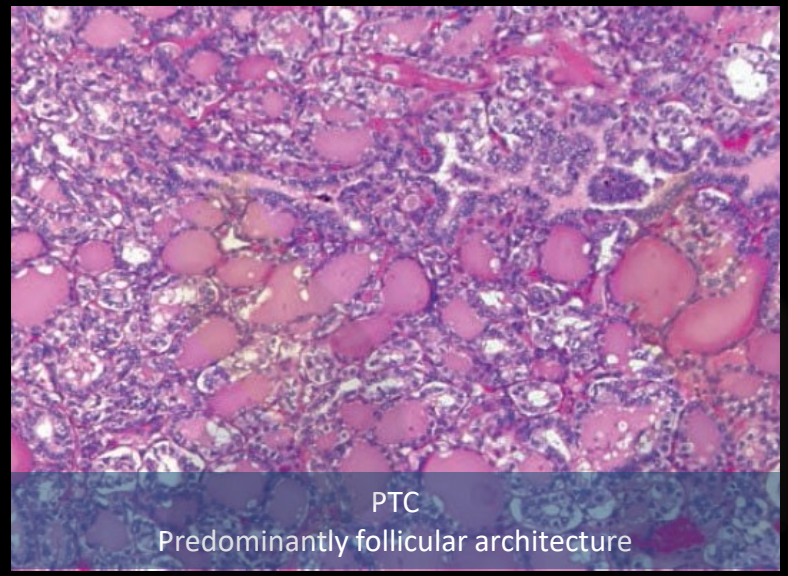
Follicular organization/Colloid formation|Follicular fraction|



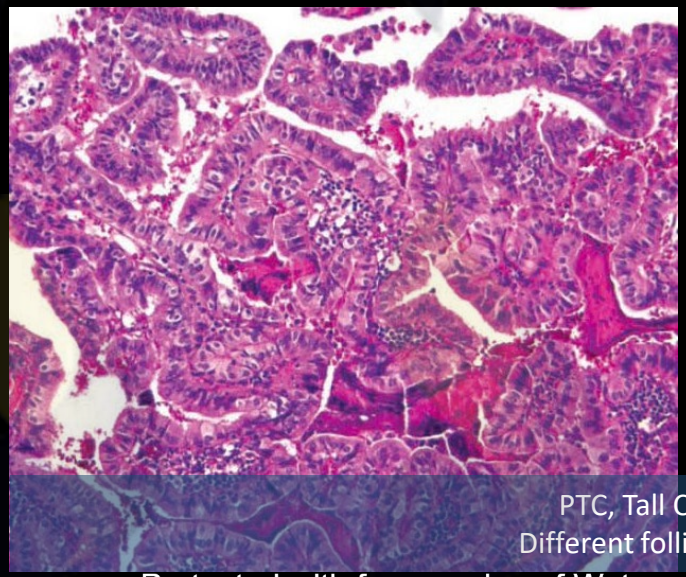
PTC, Classical,
papillary architecture with poor follicular formation

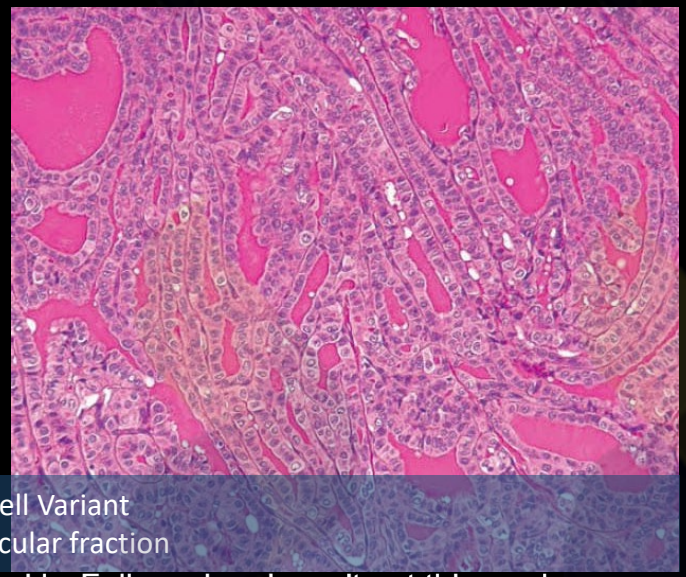


PTC, Predominantly papillary architecture
occasional neoplastic follicles



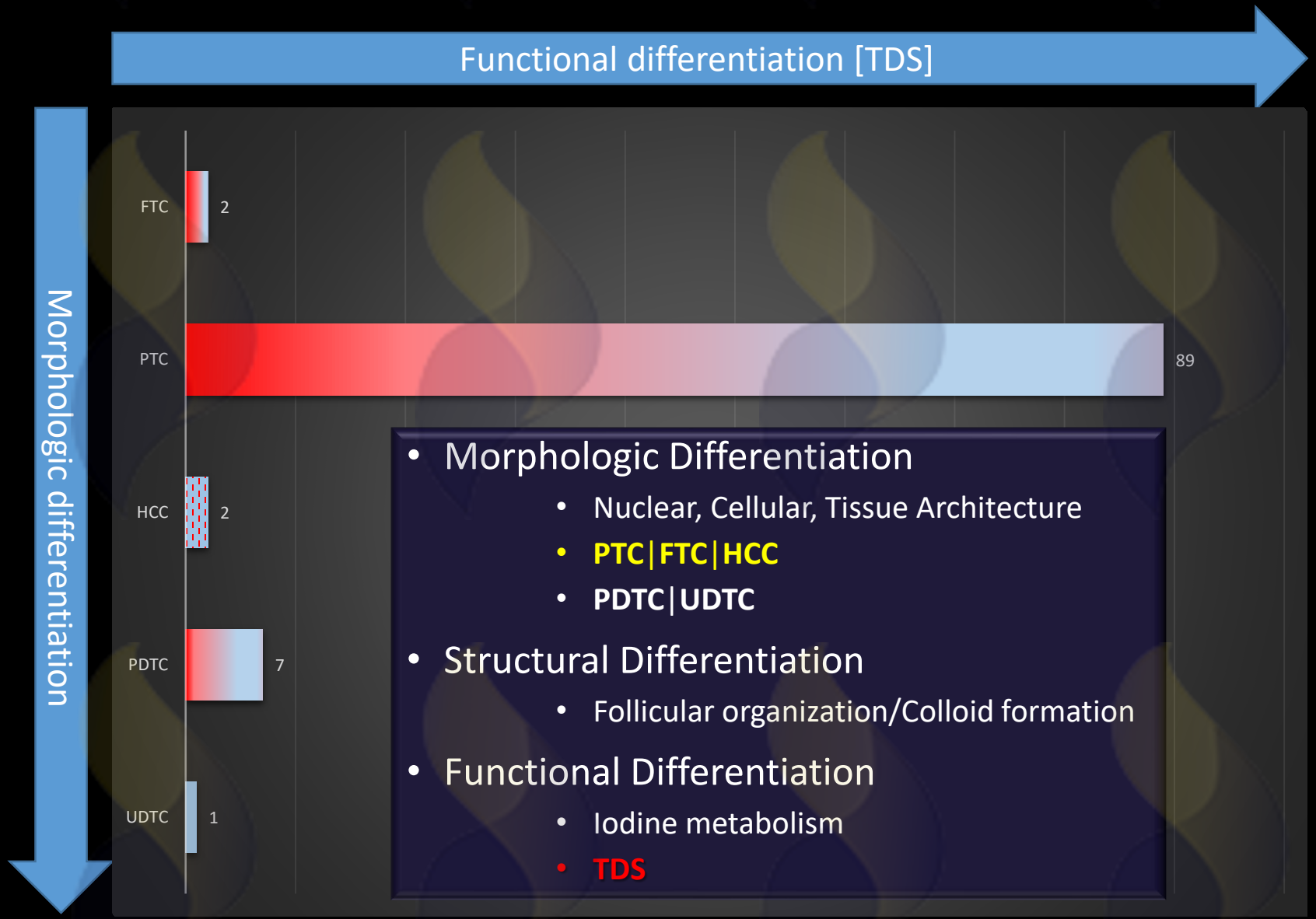
PTC
Predominantly follicular architecture



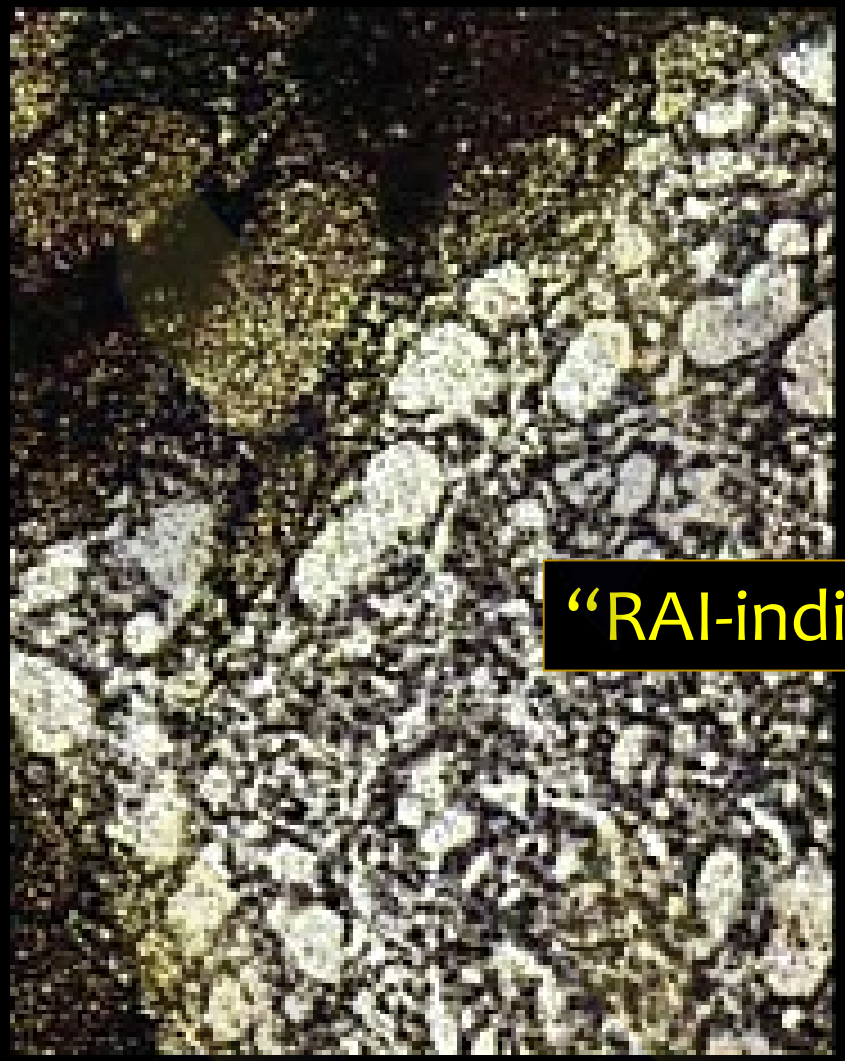


PTC, Tall Cell Variant
Different follicular fraction

Terms of Differentiation for Thyroid Cancers of Follicular Cell in Origin



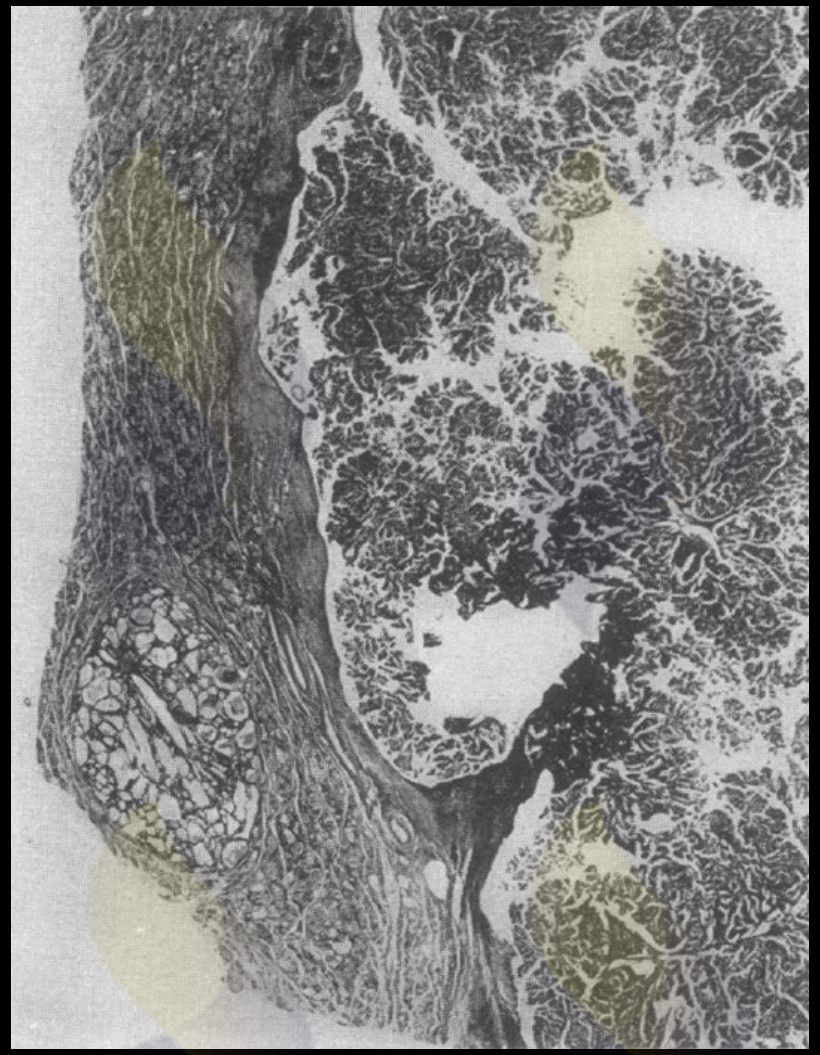
RAI uptake in “DTC”

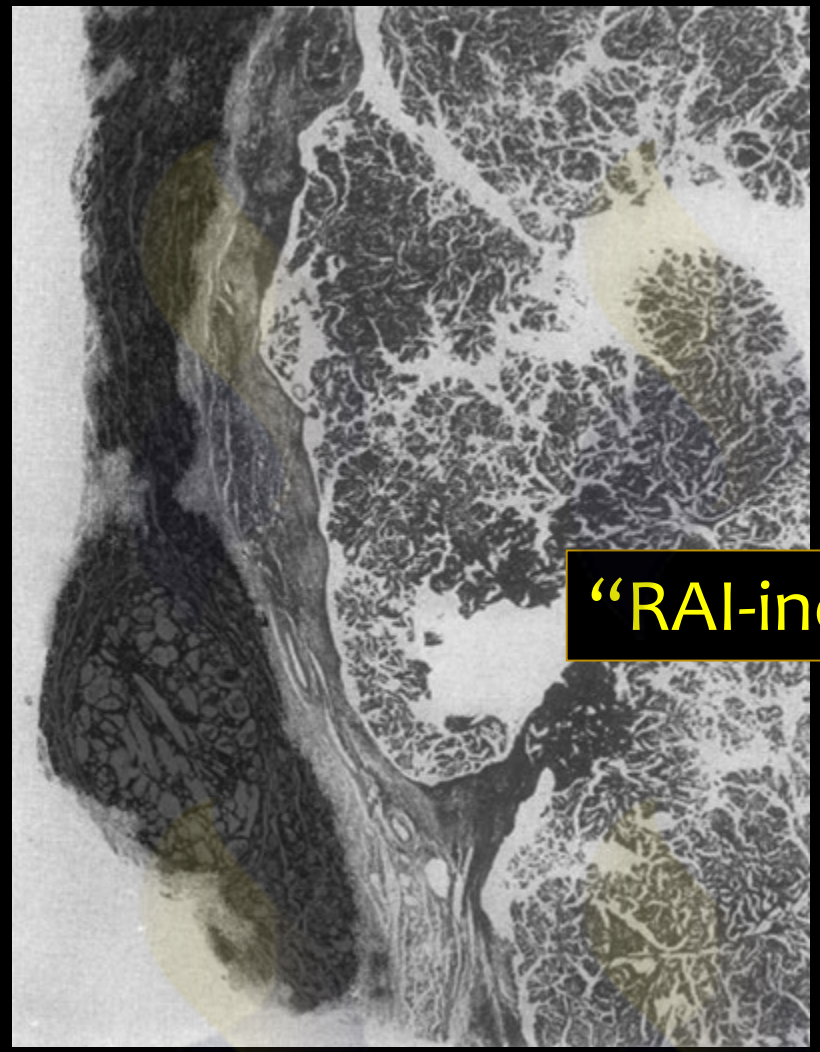


“RAI-indifferent”

Fitzgerald PJ et al. Cancer. 1950 Jan;3(1):86-105

RAI uptake in “DTC”

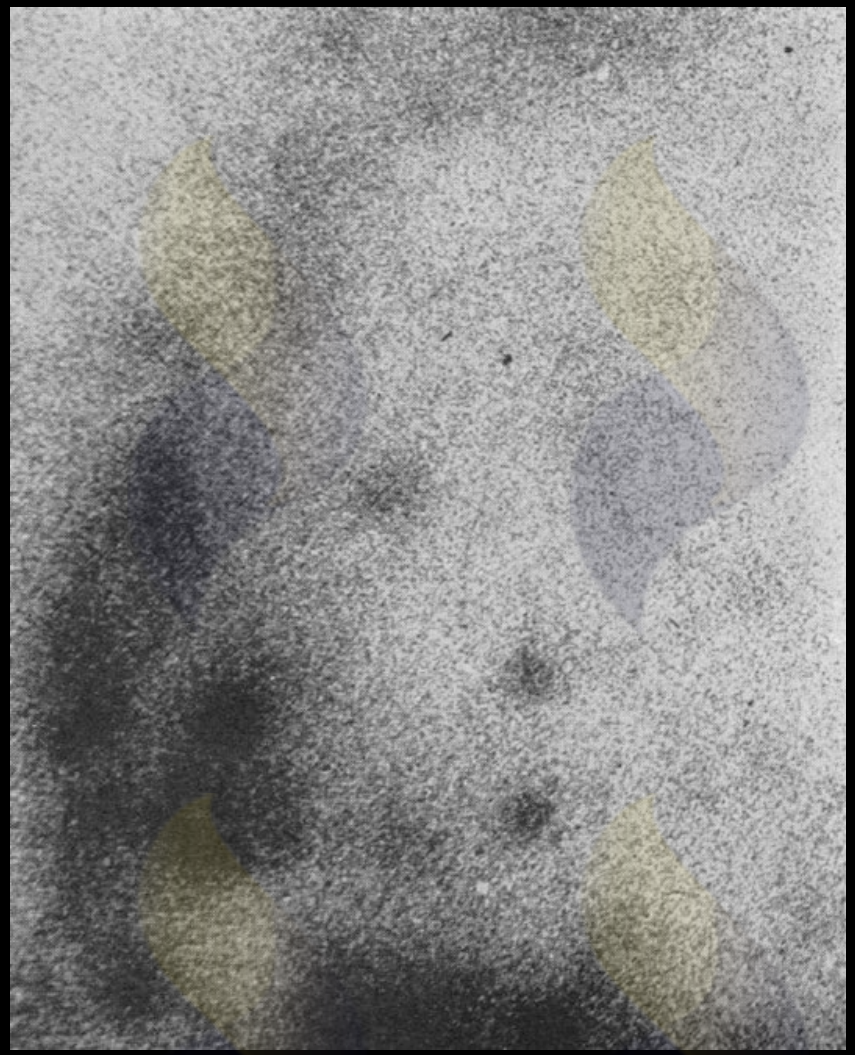


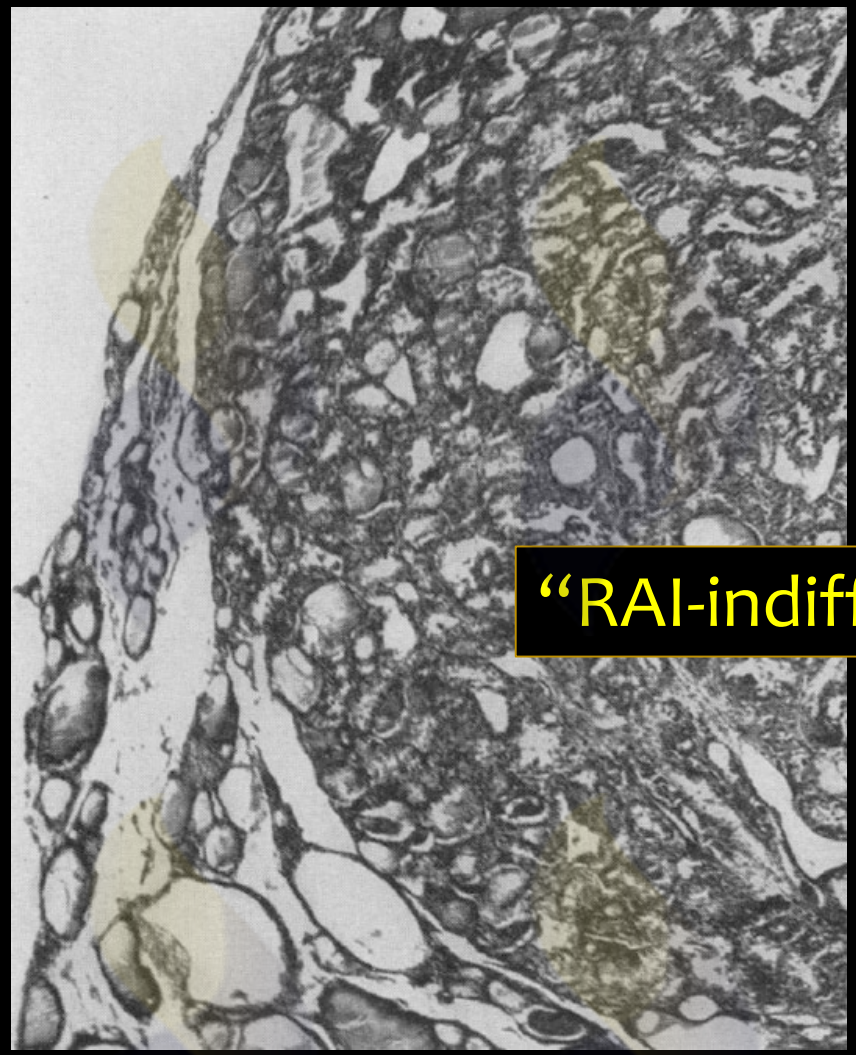


“RAI-indifferent”

Papillary carcinoma with no uptake
Surrounding normal thyroid uptake

RAI uptake in “DTC”



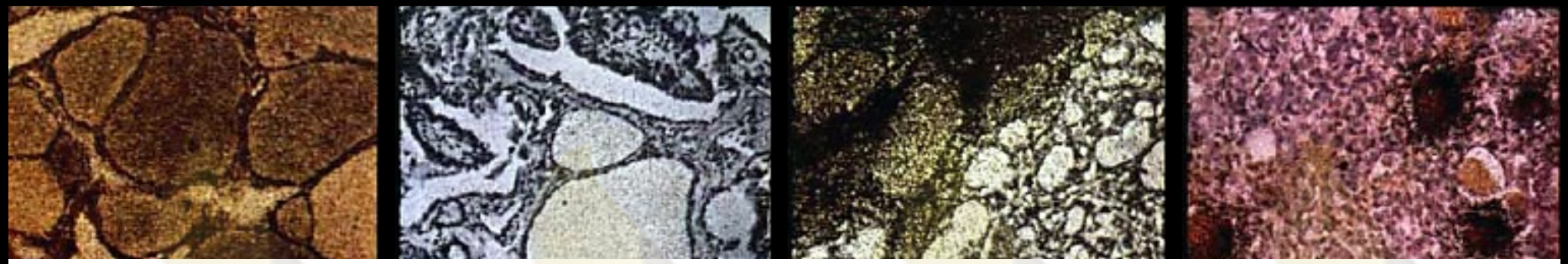


“RAI-indifferent”

Microfollicular cancer with minimal uptake

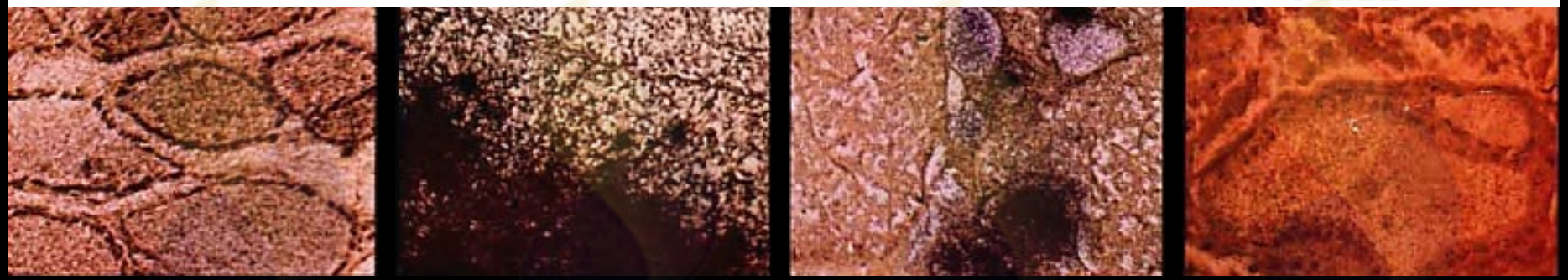
Surrounding normal uptake

A 70 years-old known unknown



RADIOAUTOGRAPHIC CONCENTRATION OF I^{131} IN 258 SEPARATE CARCINOMATOUS LESIONS

Type	Primary				Metastatic				Total			
	No.	+	%+	−	No.	+	%+	−	No.	+	%+	−
Papillary	35	4	11	31	42	16	38	26	77	20	26	57
Alveolar & follicular	44	29	66	15	67	56	84	11	111	85	77	26
Solid	12	6	50	6	16	5	31	11	28	11	39	17
Hürthle-cell	13	2	15	11	6	1	13	5	19	3	16	16
Giant- & spindle-cell	11	0	0	11	3	0	0	3	14	0	0	14
Anaplastic	1	0	0	1	5	0	0	5	6	0	0	6
Unclassified	1	0	0	1	2	2	0	0	3	2	0	1
TOTAL	117	41	35	76	141	80	57	61	258	121	47	137



Fitzgerald PJ et al. Cancer. 1950 Jan;3(1):86-135

RAI uptake in “DTC”

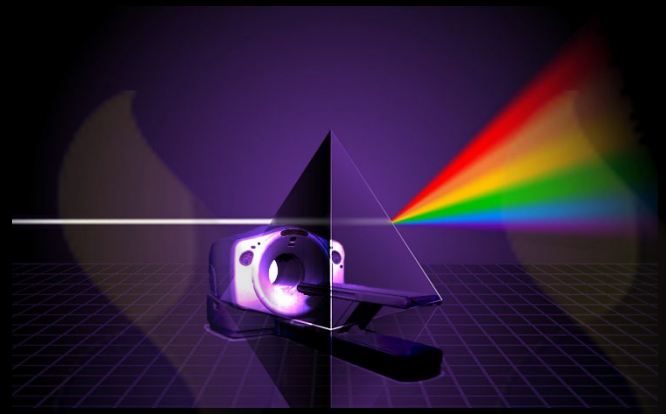
- Less than 50% of thyroid cancers pick up measurable amounts of RAI
- The tumor with the highest functional activity reported 40% of the concentrating ability of normal thyroid
- All other tumors have been reported to have RAI uptake of less than 3% of normal thyroid
- “Total thyroidectomy is the only measure proved to increase RAI uptake by metastases”

- TDS determines the theranostic Power of RAI
- TDS is inversely correlated with the MAPK-ERK output
- TDS is correlated with RAS score, but inversely correlated with BRAF score

Theranostic/Therapeutic Performance of RAI

Theranostic Power

Reversal of RAI indifference
ERK output modulation



Theranostic Performance

Theranostic Technique

Clinical protocol(s)
Optimizing RAI uptake
TSH, LID
Maximizing RAI delivery
Dosimetry

Imaging technology
Maximizing spatial resolution and quantitative accuracy
Pinhole, SPECT/CT, PET/CT

Theranostic Classification of RAI-Refractory Disease

RAI Indifference

Reversal of RAI indifference

ERK output modulation

Inadequate RAI

Clinical protocol(s)

Optimizing RAI uptake

TSH, LID

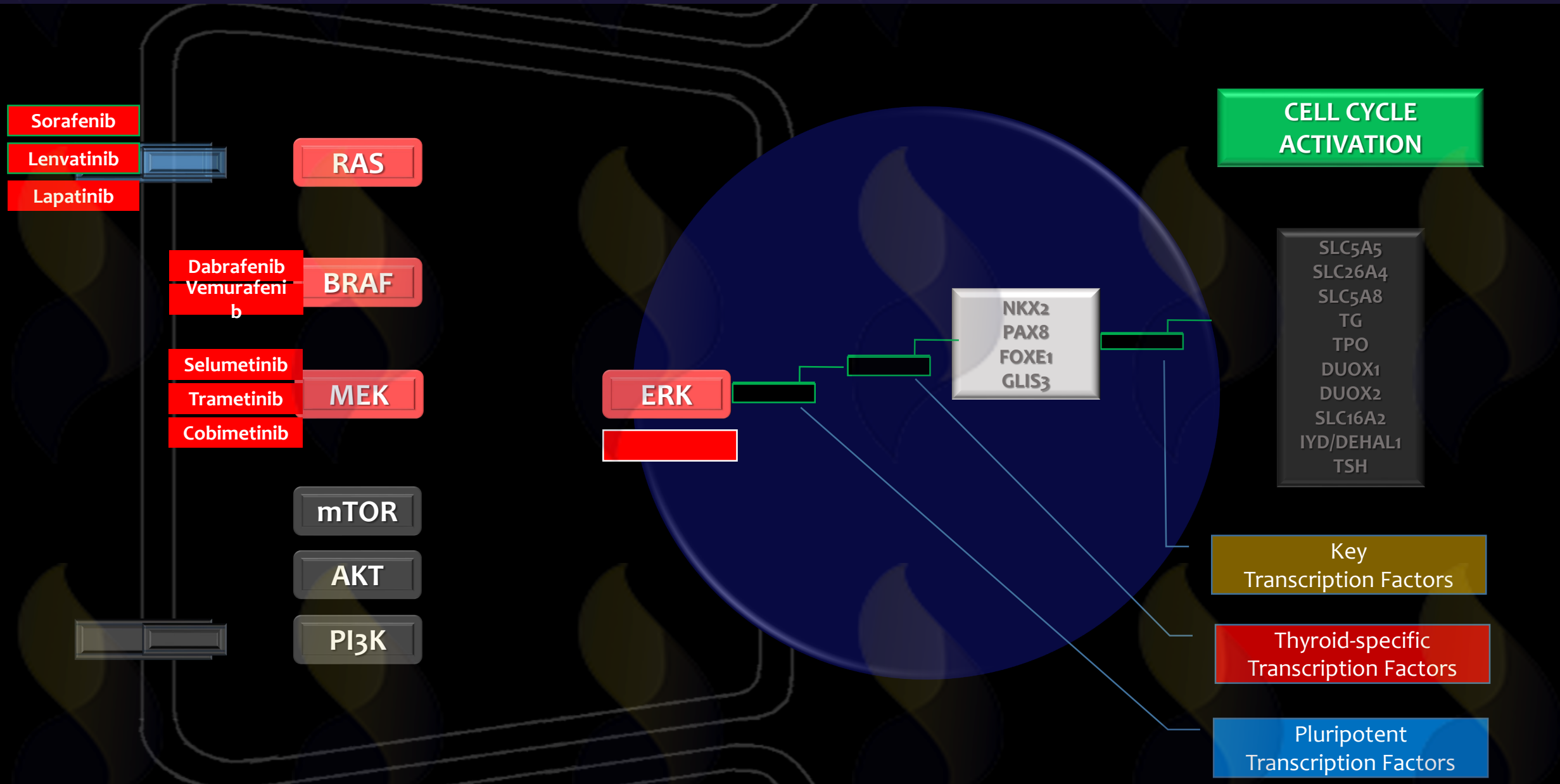
Maximizing RAI delivery

Dosimetry

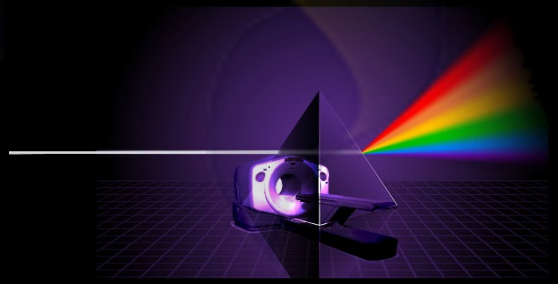
RAI Resistance

Radioresistance

MAPK pathway modulation



Multikinase inhibitors and specific kinase inhibitors



- The oncobiology of thyroid cancer attenuates the *theranostic power* of RAI
- *However, the theranostic power and performance* with RAI can be enhanced

Seza Gulec

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