CONTAMINANT-RELATED THYROID ENDOCRINE DISRUPTION IN CALIFORNIA FISH

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Pacific Coast Environmental Conservancy

501(c)3 organization

Coastal California:

intensive interfaces between marine/estuarine environments & large urban centers

San Francisco Bay Area, California

Los Angeles-Orange Counties, California

~40 years of regional environmental monitoring and research:

California's urban marine & estuarine environments are contaminated by a wide variety of anthropogenic chemicals

Which of these environmental contaminants have deleterious effects in wildlife?

Animal Phenotypic Response Measurements

as methodology in understanding environmental (water quality) effects

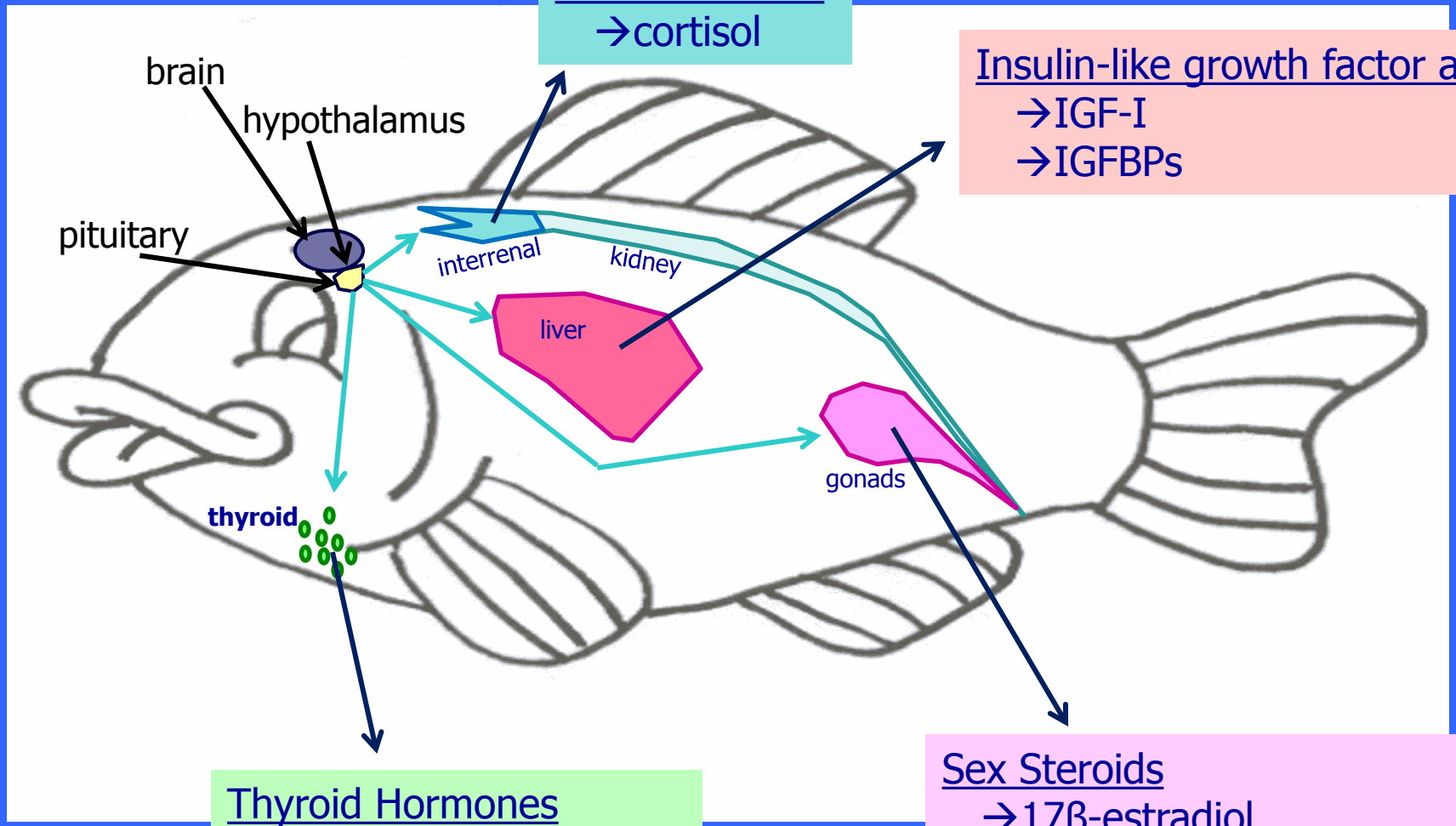
Endocrine Responses

[environmental endocrinology]

Tissue Expression Responses

[proteomics, genomics]

"Disruptable" Endocrines Documented in Coastal California Fish



Glucocorticoids
→cortisol

Insulin-like growth factor axis
→IGF-I
→IGFBPs

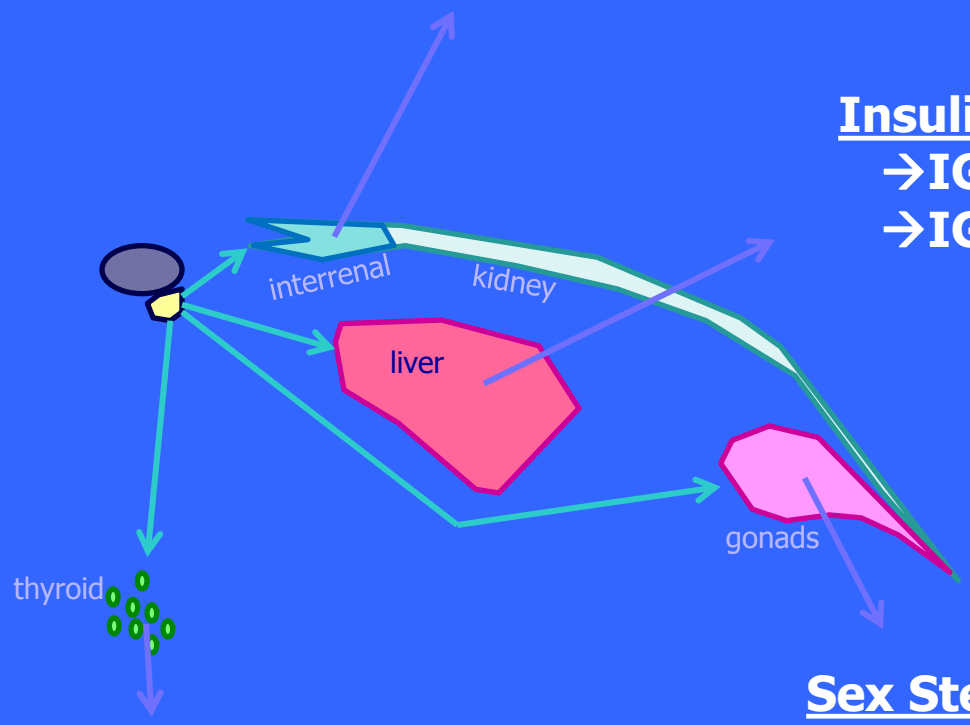
Thyroid Hormones
→thyroxine (T4)
→triiodothyronine (T3)

Sex Steroids
→17β-estradiol
→estrone
→11-ketotestosterone (11-KT)
→testosterone

Consequence

Glucocorticoids
→cortisol

fuel metabolism, osmoregulation, immune & defense, growth, behavior, stress response



Insulin-like growth factor axis
→IGF-I
→IGFBPs

growth, tissue repair, osmoregulation

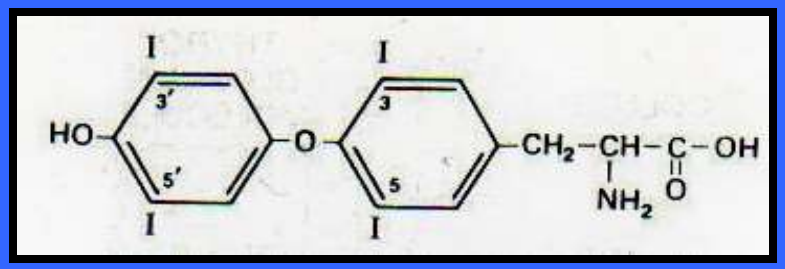
Thyroid Hormones
→thyroxine (T4)
→triiodothyronine (T3)

Sex Steroids
→17β-estradiol
→estrone
→11-ketotestosterone (11-KT)
→testosterone

reproductive physiology and behavior

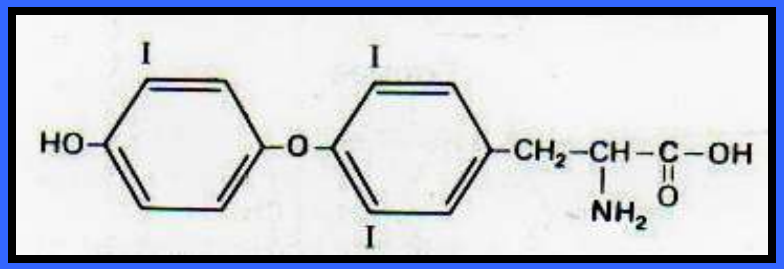
Thyroid Endocrine System

T4



3,5,3',5'-tetraiodothyronine (thyroxine)

T3



3,5,3'-triiodothyronine

- *broad physiological actions*
- essential for brain/neural development
- permissive to somatic growth
- important regulators of metabolism

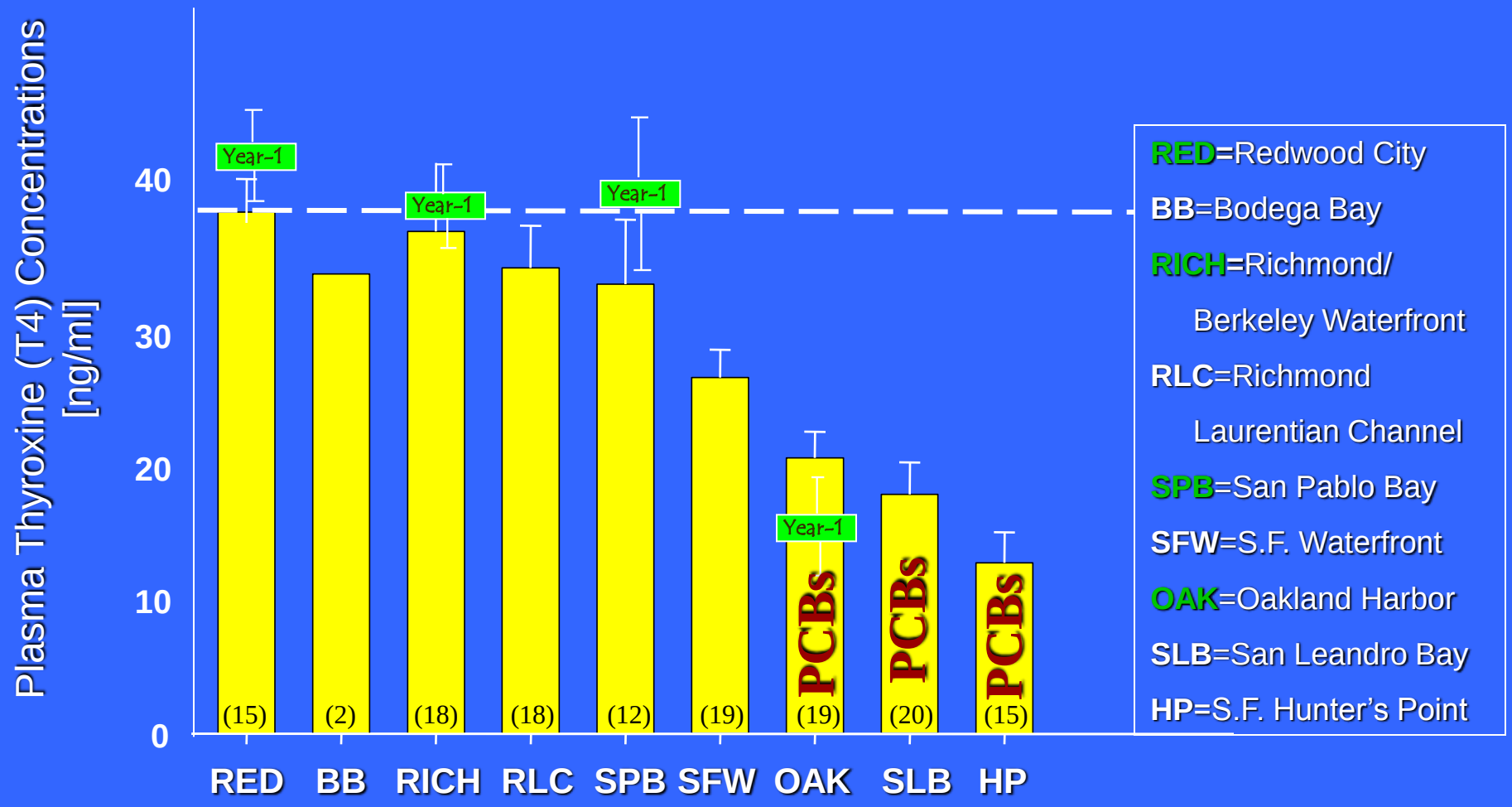
Shiner perch

Cymatogaster aggregata

Pacific Staghorn Sculpin

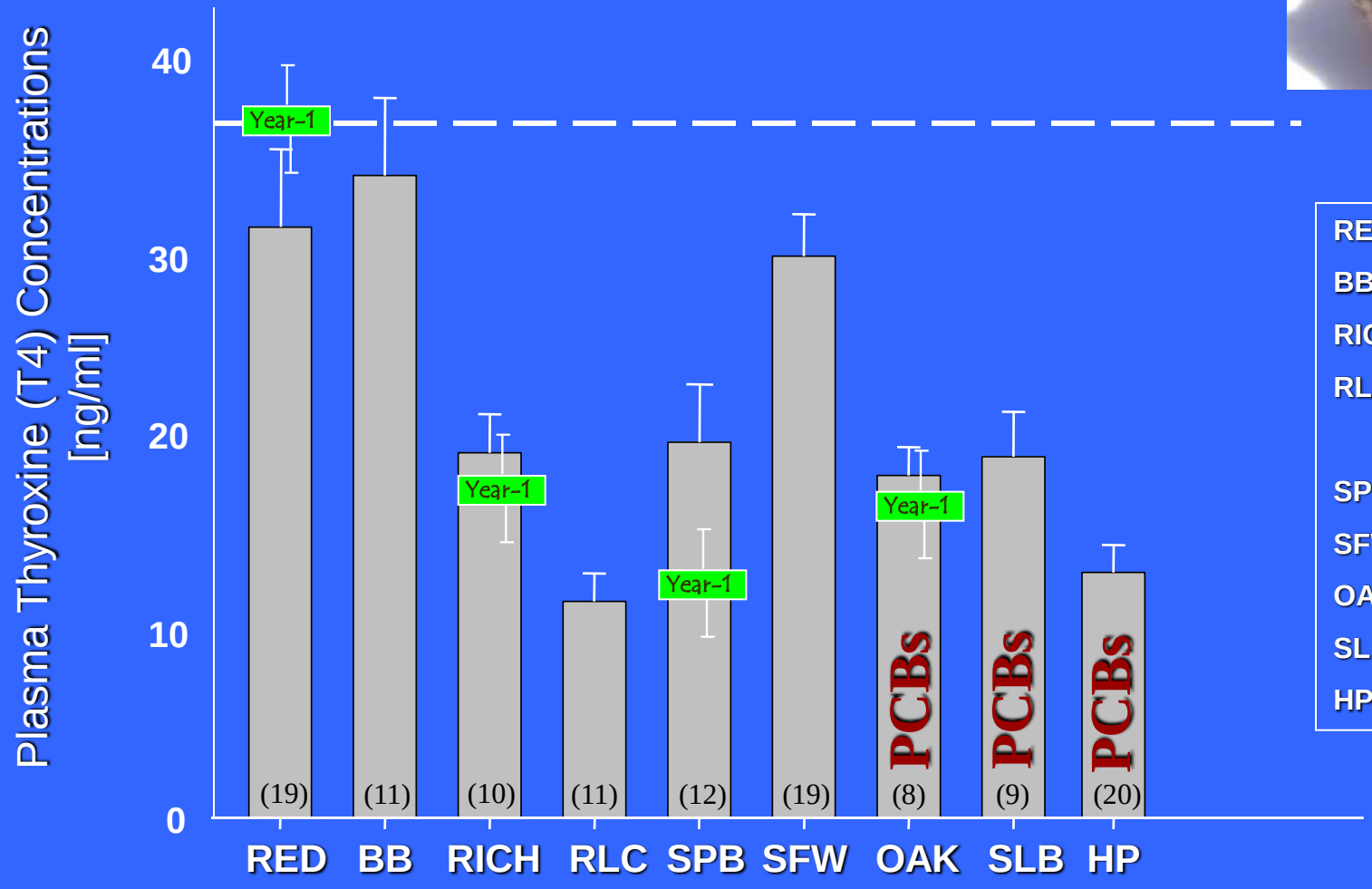
Leptocottus armatus

Thyroxine Levels in SF Bay Fish



Brar *et al.*, 2010, *Aquatic Toxicology*

Thyroxine Levels in SF Bay Fish



RED=Redwood City
BB=Bodega Bay
RICH=Richmond W-F
RLC=Richmond Laurentian Channel
SPB=San Pablo Bay
SFW=S.F. Waterfront
OAK=Oakland Harbor
SLB=San Leandro Bay
HP=S.F. Hunter's Point

Brar *et al.*, 2010, *Aquatic Toxicology*

Potential Mechanisms Underlying Effect?

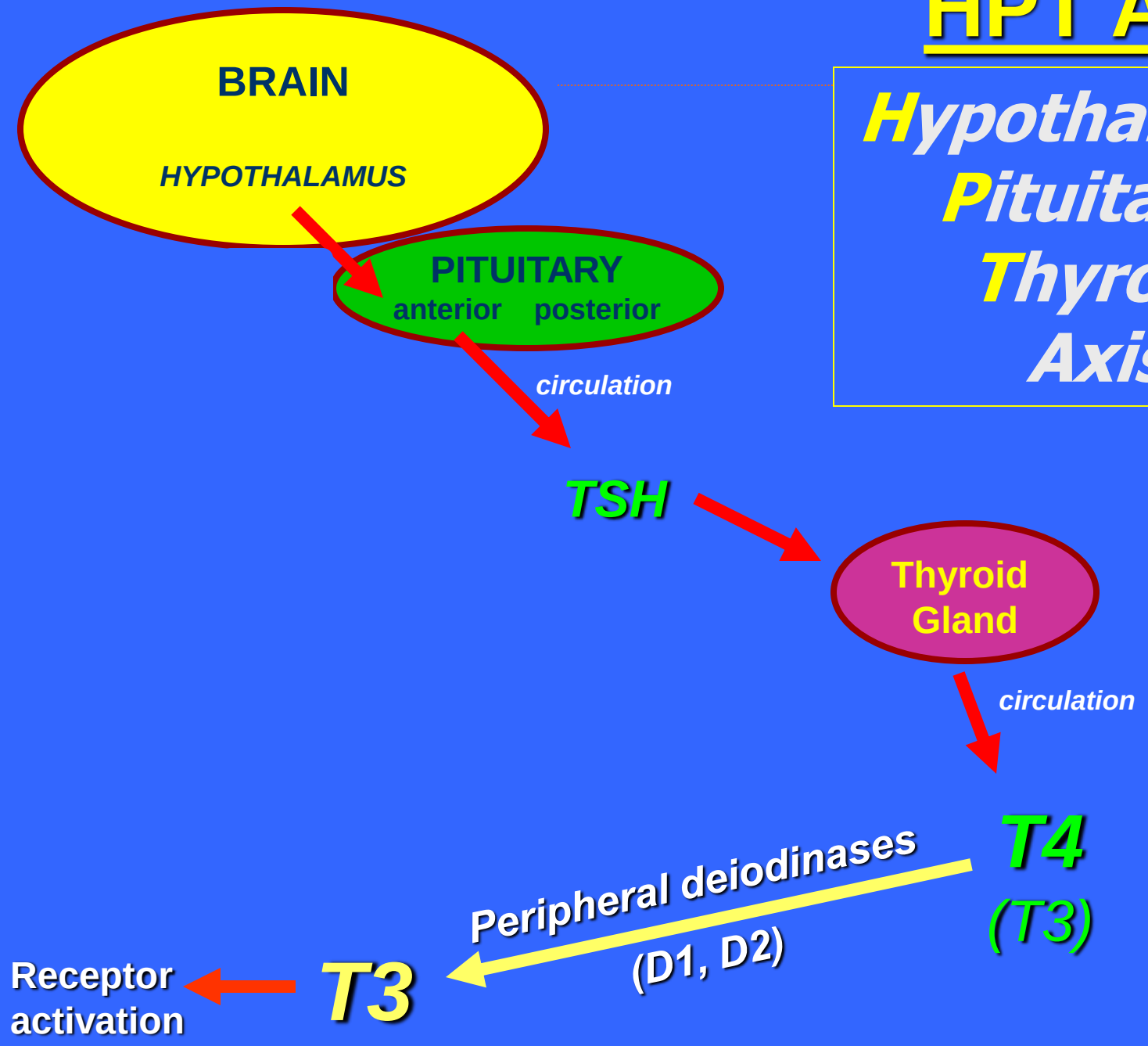
OAK vs. RED

Oakland Harbor

Redwood City

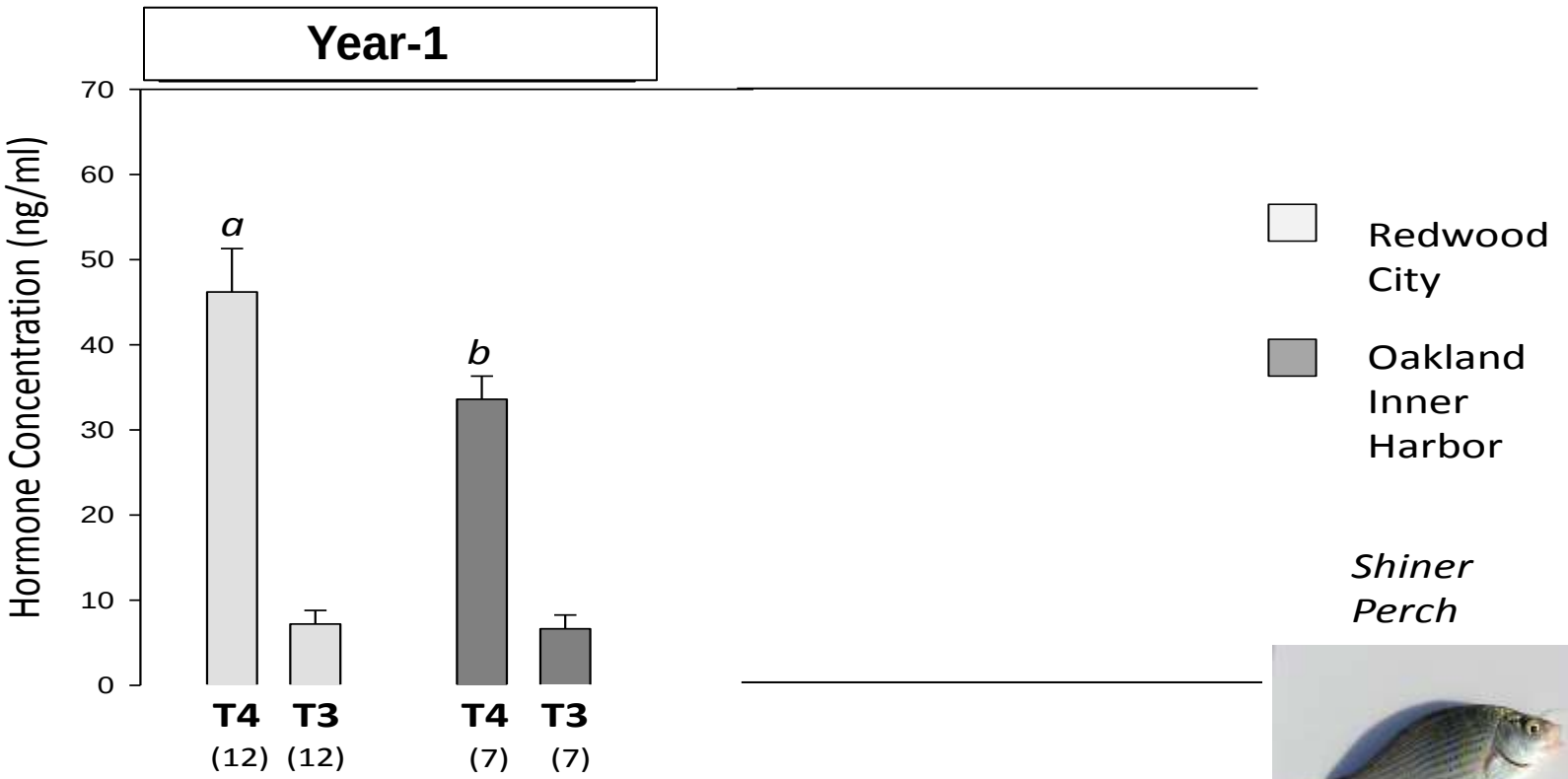
HPT Axis

Hypothalamo-Pituitary-Thyroid Axis



Shiner perch
Cymatogaster aggregata

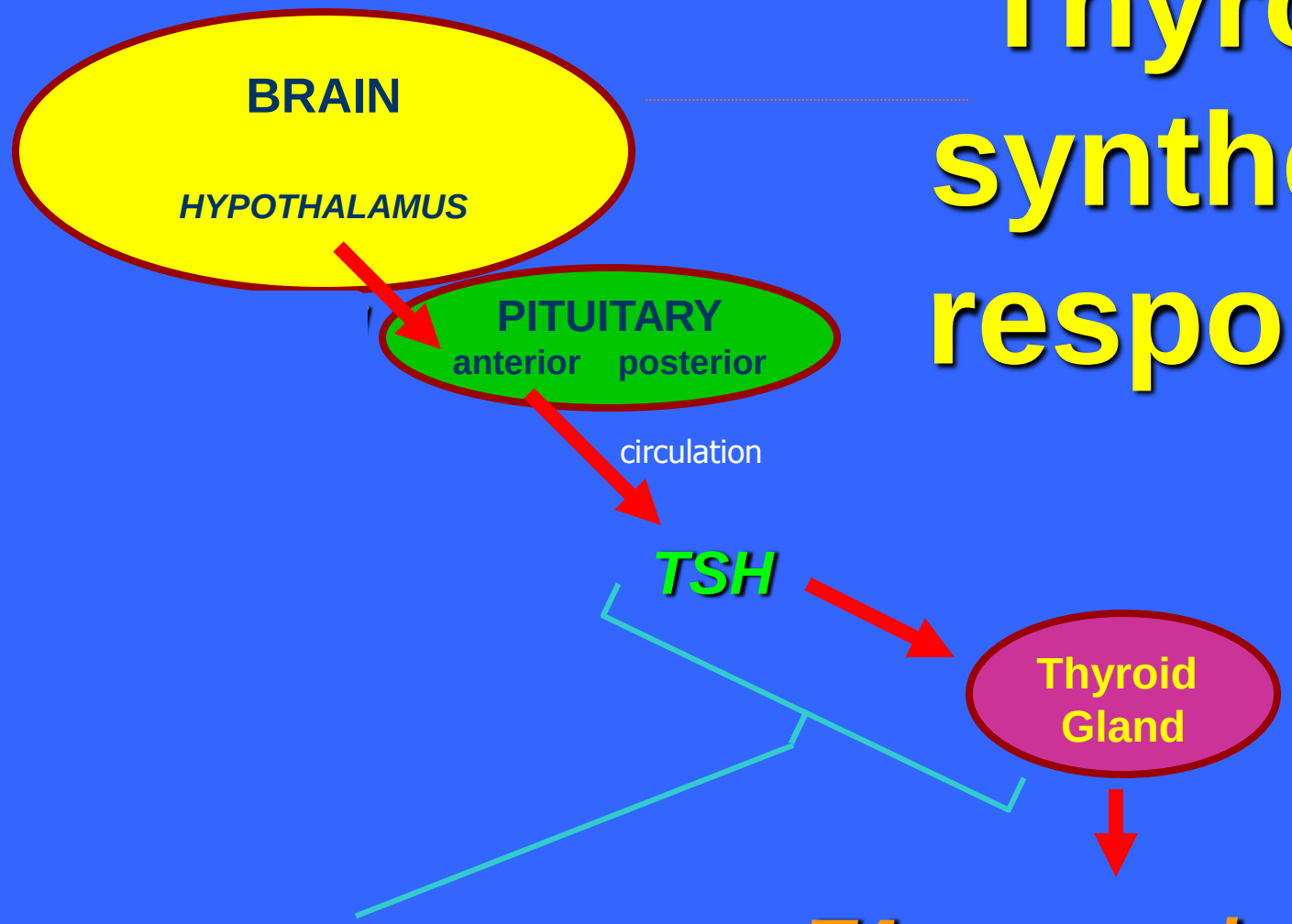
T4 and T3 Concentrations in Fish from Redwood City *(ref)* and Oakland *(impacted)*



Shiner Perch

Lack of difference in T3 suggests no effect on 5'-deiodinase activity

Thyroid synthetic response



TSH challenge to test thyroid synthetic response

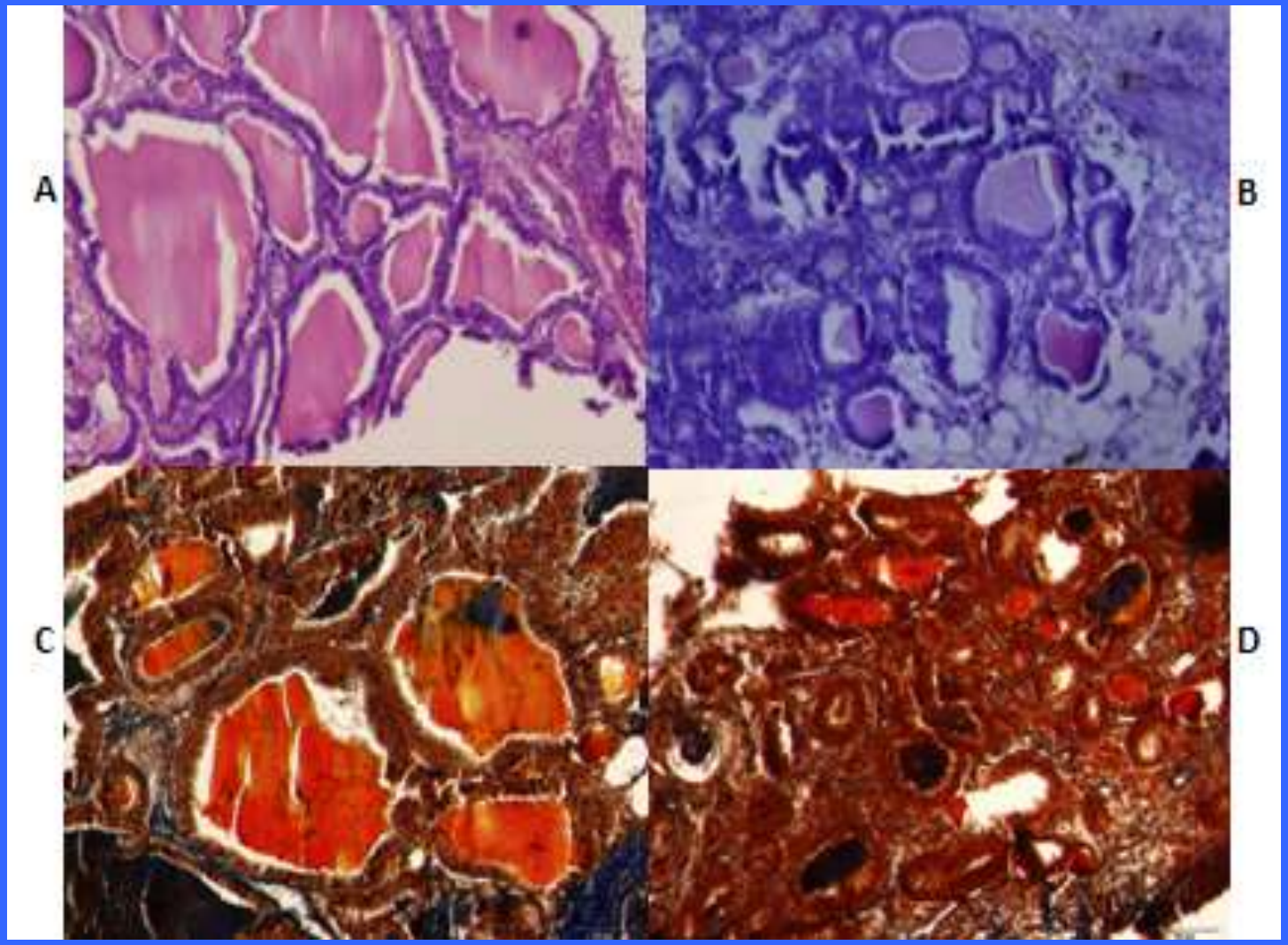
T4 *(T3)* ***production***

physiological actions

Thyroid Response to TSH Challenge in Fish from Redwood City *(ref)* and Oakland *(impacted)*

(0.5 µg TSH / g BW, 2 hr)

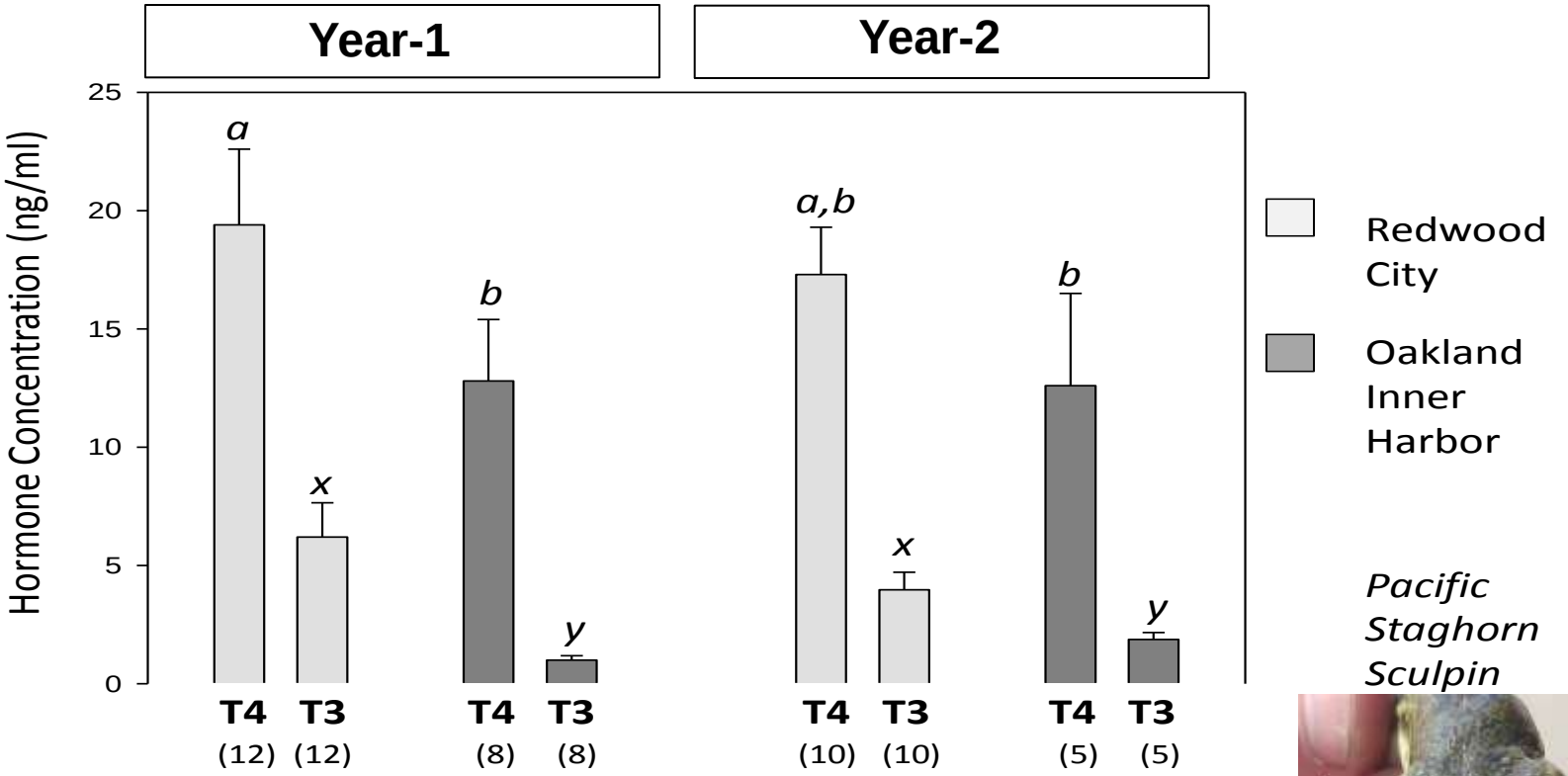
Shiner Perch



Shiner perch thyroid tissue. The two upper tissues are stained with hematoxylin and eosin (A, B) and the two bottom tissues are stained using the Mallory trichrome Stain. Shiner perch sampled from OAK (B, D) exhibit disorganized morphology and severely reduced colloid volumes in comparison to shiner perch sampled from RED (A, C).

Pacific Staghorn Sculpin
Leptocottus armatus

T4 and T3 Concentrations in Fish from Redwood City *(ref)* and Oakland *(impacted)*

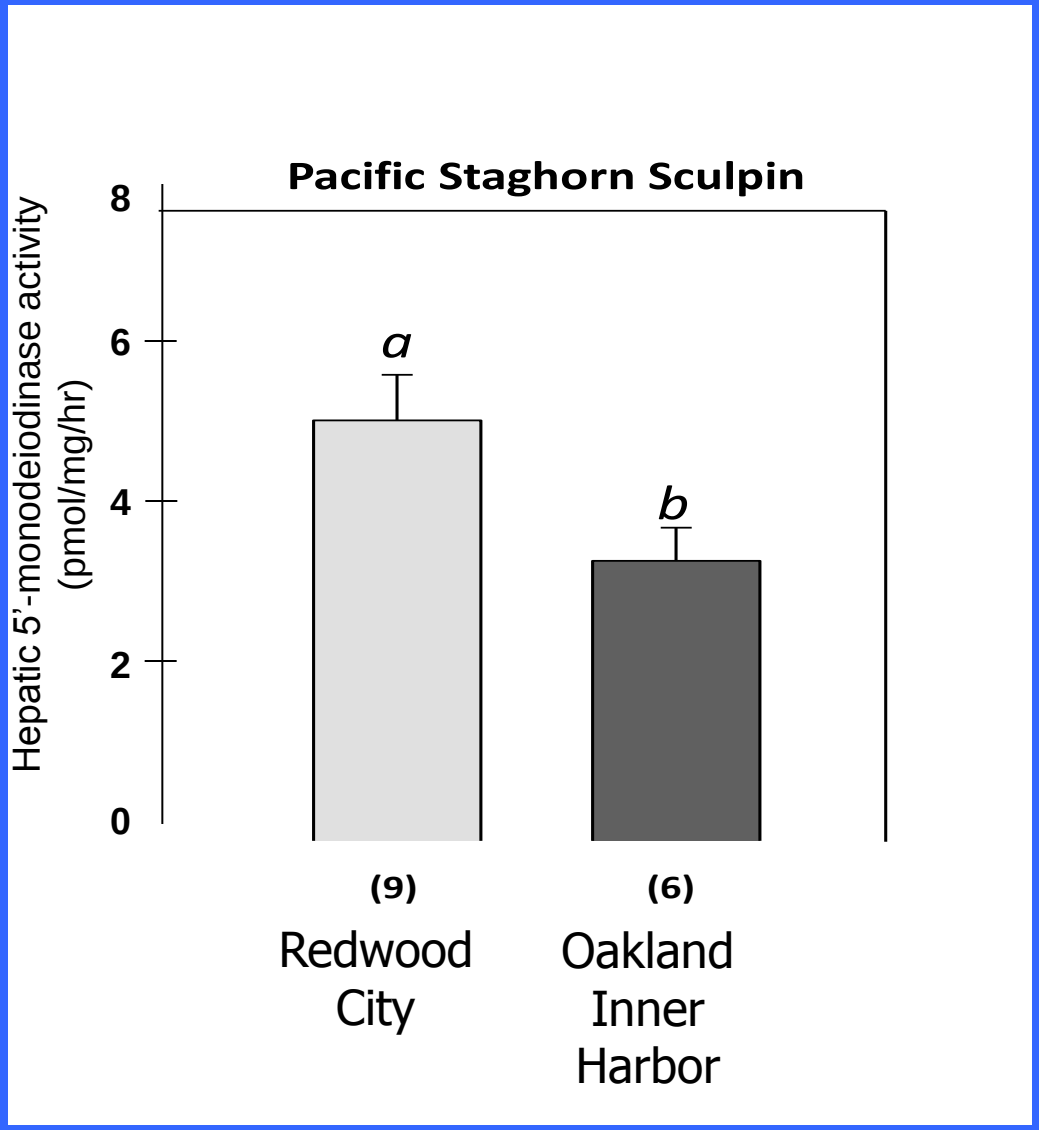


Pacific Staghorn Sculpin

Differences in T3 suggest effect on 5'-deiodinase activity

Hepatic 5'-Monodeiodinase Activity in Wild Fish

Redwood City *(reference)* *vs.* Oakland Harbor *(impacted)*



Thyroid Endocrine Disruption & Contaminant Exposures

Brar et al. (2010) *Aquatic Toxicology*

reduced T4
related to PCB exposures

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putative mechanism:

impaired thyroid synthesis of T.H.

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Phenol
2-Chlorophenol
Aniline
2,4-Dimethylphenol
bis(2-Chloroethoxy) methane
1,3-Dichlorobenzene
1,4-Dichlorobenzene
1,2-Dichlorobenzene
Benzyl Alcohol
2-Nitrophenol
bis(2-Chloroisopropyl) ethane
2,4-Dichlorophenol
N-nitrosodi-n-propylamine
N-nitrosodimethylamine
Hexachloroethane
Nitrobenzene
Naphthalene
Isophorone
Dichlorvos
bis(2-Chloroethyl) ether
1,2,4-Trichlorobenzene
Benzidine
4-Chloro-3-methylphenol
4-Chloroaniline
2-Methylnaphthalene
Hexachlorobutadiene
1-Methylnaphthalene
2,4,6-Trichlorophenol
Benzoic Acid
Biphenyl

2,6-Dimethylnaphthalene
Mevinphos
Hexachlorocyclopentadiene
Acenaphthylene
Dimethyl Phthalate
Acenaphthene
4-Nitroaniline
2,4-Dinitrophenol
4-Nitrophenol
2,3,5-Trimethylnaphthalene
Fluorene
Diethyl Phthalate
2,6-Dinitrotoluene
2-Methyl-4,6-dinitrophenol
Dibenzofuran
Demeton
2,4-Dinitrotoluene
Ethoprop
4-Chlorophenyl phenyl ether
2-Nitroaniline
Phorate
N-nitrosodiphenylamine
Azobenzene
Dimethoate
Pentachlorophenol
Phenanthrene
4-Bromophenyl phenyl ether
Anthracene
alpha-BHC
Diazinon

Disulfoton
Hexachlorobenzene
beta-BHC
gamma-BHC
Methyl Parathion
delta-BHC
Fenchlorophos
1-Methylphenanthrene
Dibutyl Phthalate
Malathion
Fenthion
Chlorpyrifos
Heptachlor
Trichloronate
Fluoranthene
Tokuthion
Heptachlor Epoxide
Bolstar
gamma-Chlordane
2,4'-DDE
alpha-Chlordane
Fensulfothion
trans-Nonachlor
4,4'-DDE
Merphos
Dieldrin
2,4'-DDD
Butylbenzyl Phthalate
Endrin
Endosulfan II

4,4'-DDD
2,4'-DDT
Endrin Aldehyde
Benz[a]anthracene
Chrysene
Endosulfan Sulfate
4,4'-DDT
bis-(2-ethylhexyl) Phthalate
Endrin Ketone
Guthion
Coumaphos
Methoxychlor
Mirex
Di-n-octyl Phthalate
Benzo[b]fluoranthene
Benzo[k]fluoranthene
Benzo[e]pyrene
Benzo[a]pyrene
Perylene
3,3'-Dichlorobenzidine
Indeno[1,2,3-c,d]pyrene
Dibenz[a,h]anthracene
Benzo[g,h,i]perylene
Aldrin
Pyrene
Tetrachlorvinphos
3-Nitroaniline
Endosulfan I
PCBs By Congener
PCBs By Aroclor

PCB 18	PCB 28	PCB 37	PCB 44	PCB 49
PCB 52	PCB 66	PCB 70	PCB 74	PCB 77
PCB 81	PCB 87	PCB 87	PCB 99	PCB 101
PCB 105	PCB 110	PCB 114	PCB 118	PCB 119
PCB 123	PCB 126	PCB 128	PCB 138	PCB 149
PCB 151	PCB 153	PCB 156	PCB 157	PCB 158
PCB 167	PCB 168	PCB 169	PCB 170	PCB 177
PCB 180	PCB 183	PCB 187	PCB 189	PCB 194
PCB 200	PCB 201	PCB206		

D5-Phenol (Recovery Surrogate)
PCB112 (Recovery Surrogate)
Phenanthrene-d10 (Recovery Surrogate)
2,4,6-Tribromophenol (Recovery Surrogate)
PCB198 (Recovery Surrogate)

Acenaphthene-d10 (Recovery Surrogate)
Naphthalene-d8 (Recovery Surrogate)
2,2'-5,5'-Tetrabromobiphenyl (Internal Standard)
Anthracene-d10 (Internal Standard)
Perylene-d12 (Recovery Surrogate)

PCB030 (Recovery Surrogate)
2,4,5,6-Tetrachloro-m-xylene (Recovery Surrogate)
2-Fluorophenol (Recovery Surrogate)
Chrysene-d12 (Recovery Surrogate)

Thyroid Endocrine Disruption & Contaminant Exposures

Brar et al. (2010) *Aquatic Toxicology*

relative T3 levels
related to chlorinated pesticide exposures
(chlordanes, DDT)

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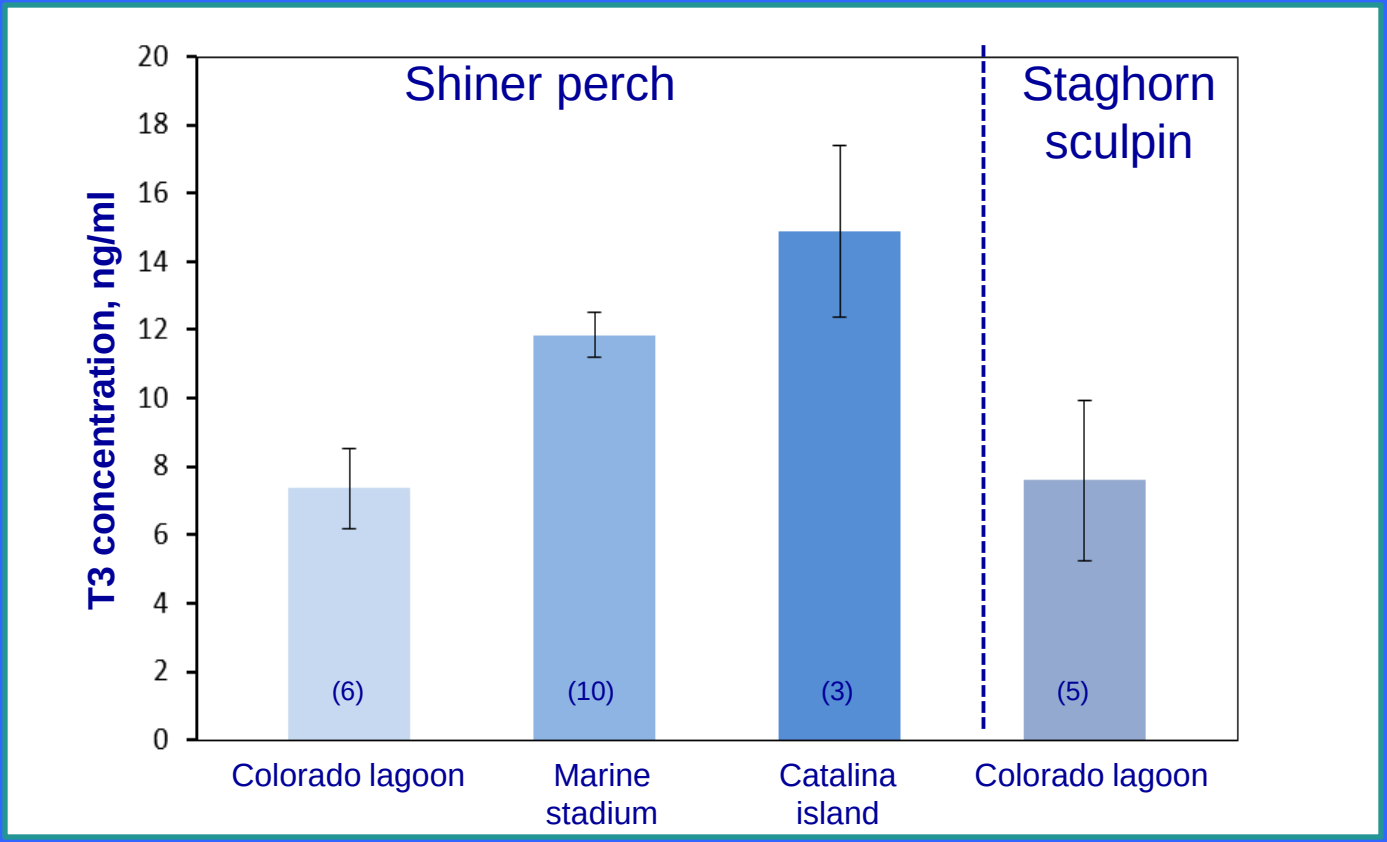
putative mechanism:

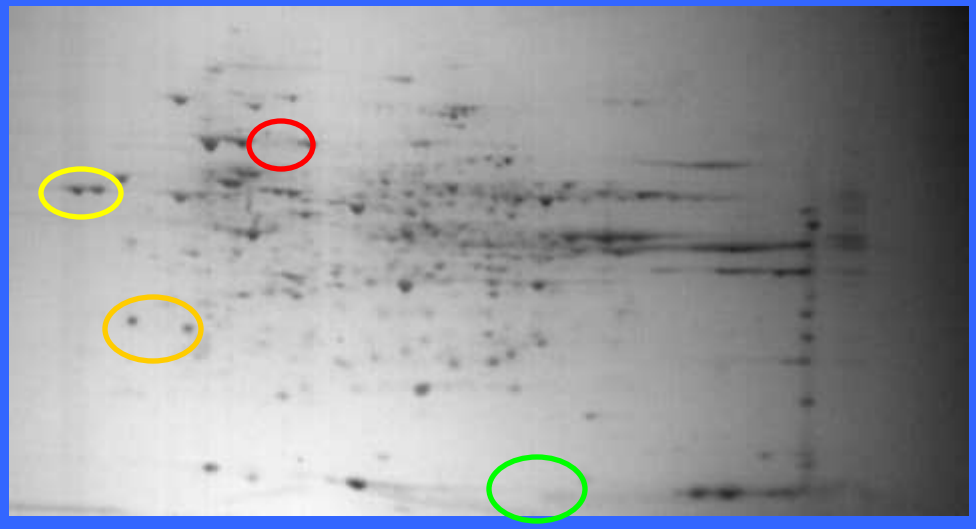
altered peripheral 5'-monodeiodinase

Colorado Lagoon

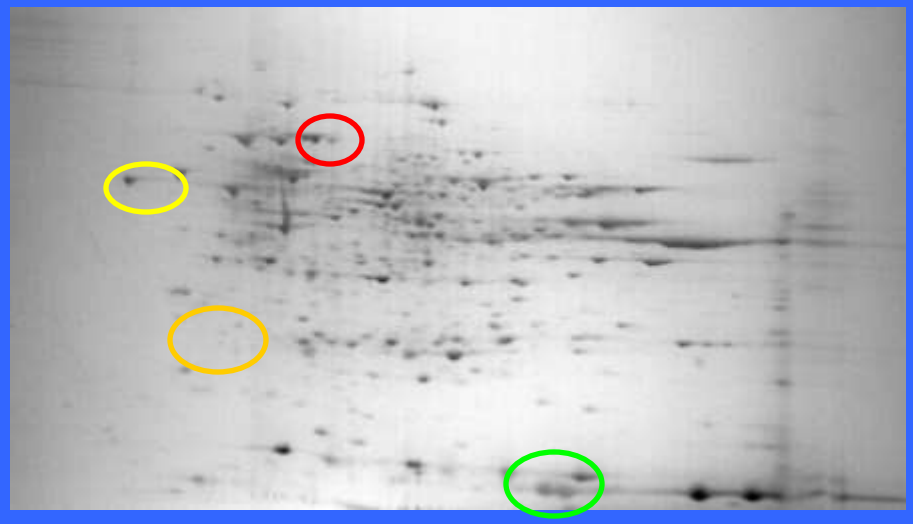
Colorado lagoon
T3 hormone levels



Proteomic comparison

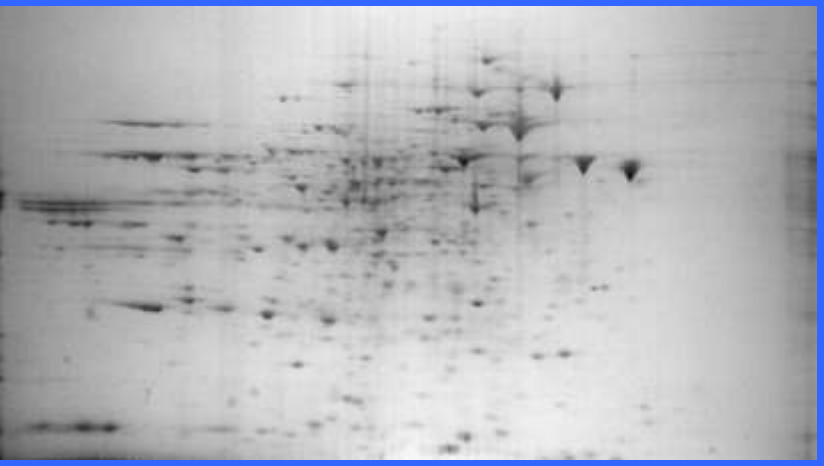


Colorado lagoon

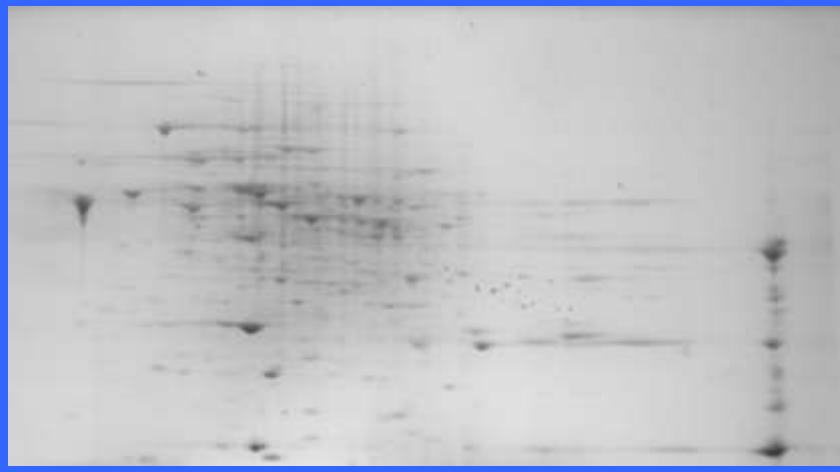


Redwood city

Proteomic comparison



Colorado lagoon



Redwood city

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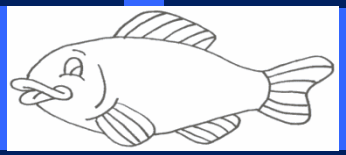
Environmental Chemistry

Endocrinology & Toxicology



Proteomics & Environmental Biology

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Multiple Measures Approach

Acknowledgements

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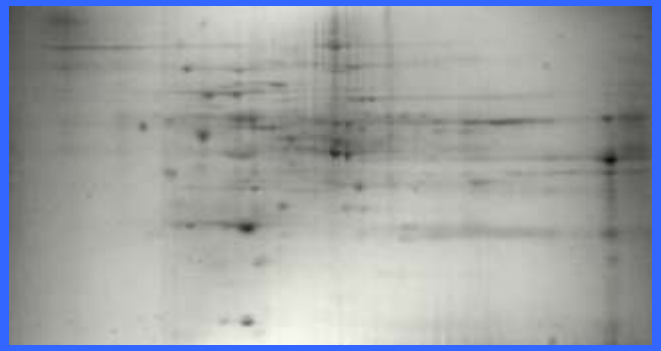
Dwight Causey, Ricky Patel, Navdeep Brar, Claire Waggoner and Andrew Hamilton

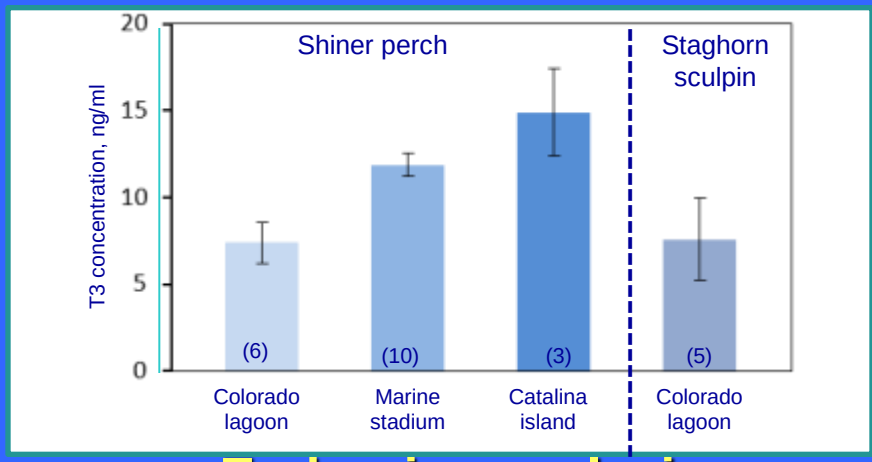
?'s

Multi Biomarker Approach



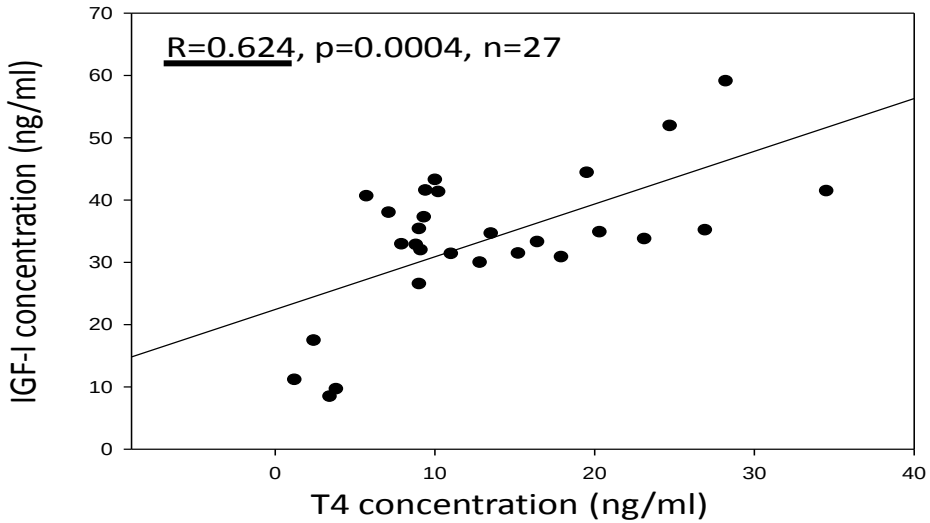
Protein profiling/identification

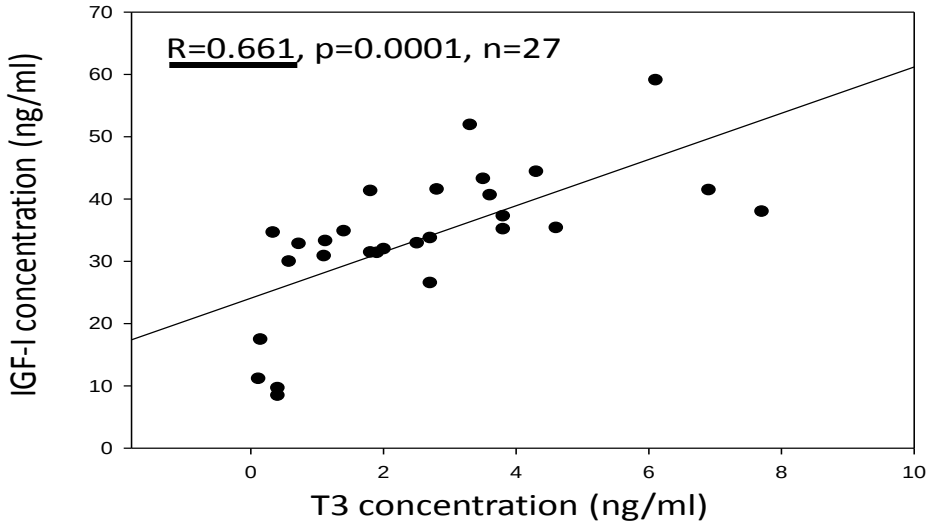
Contaminant Measurements



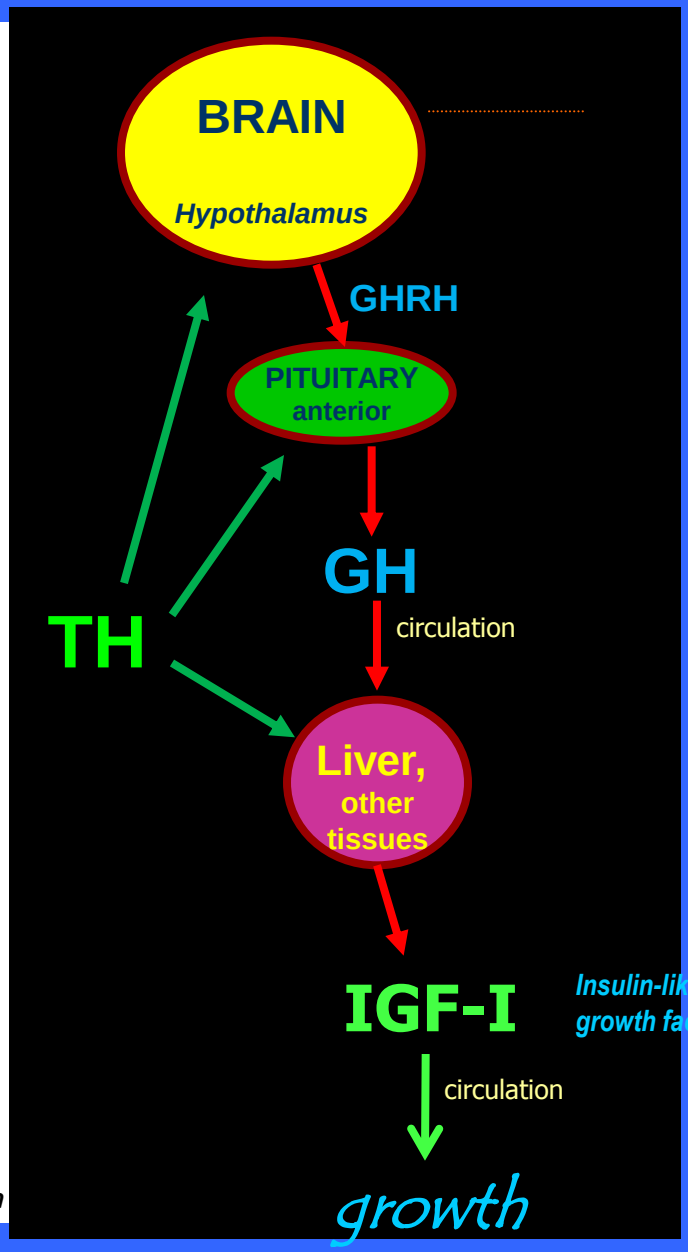
Endocrine analysis

Thyroid Disruption & Fish Growth?

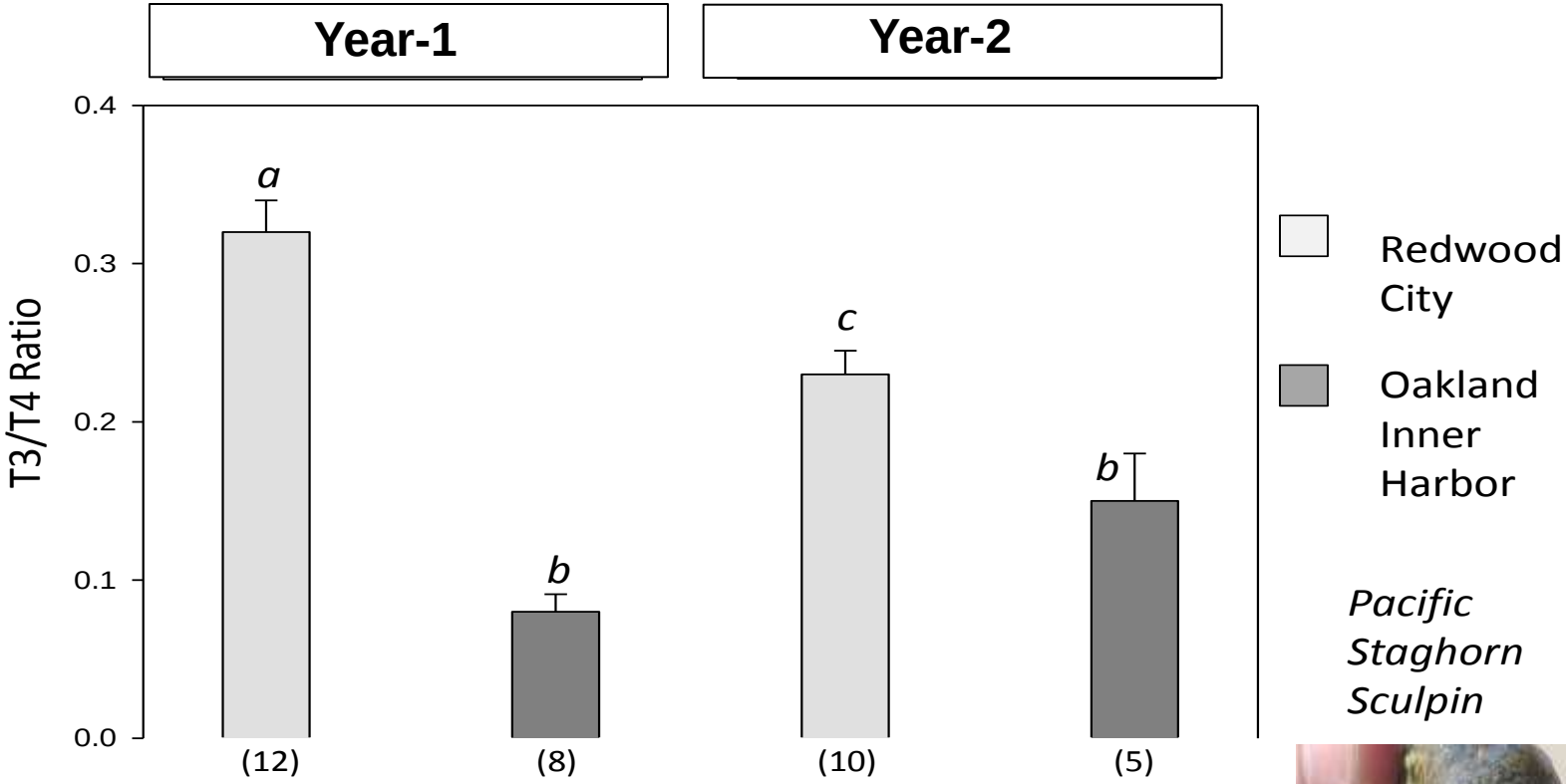




Pacific staghorn sculpin



T3/T4 Ratio in Fish from Redwood City *(ref)* and Oakland *(impacted)*



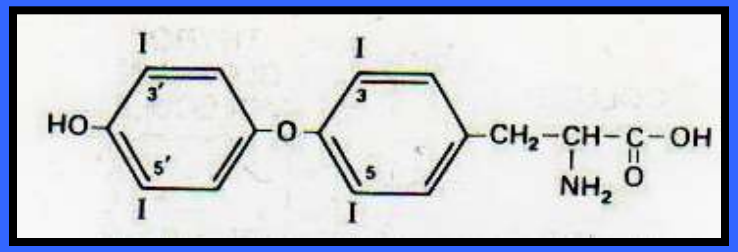
Pacific Staghorn Sculpin

Differences in T3/T4 ratio suggest effect on 5'-deiodinase activity

Hepatic 5'-Deiodinase Activity

(after Leatherland et al., 1990s)

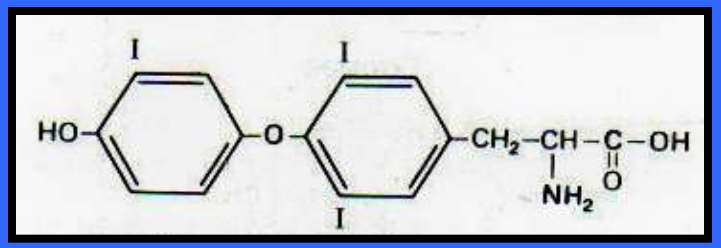
T4



3,5,3',5'-tetraiodothyronine (thyroxine)

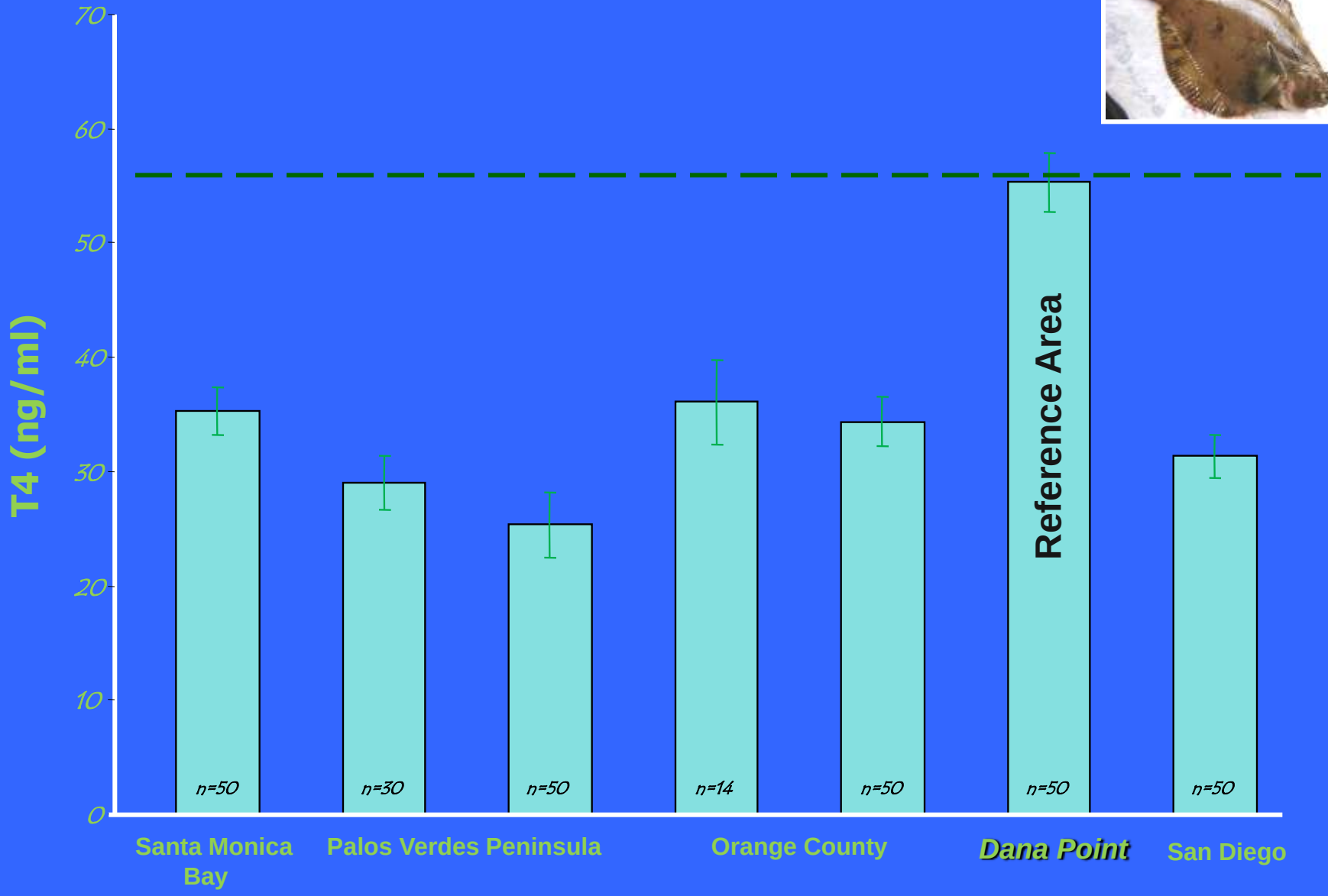
iodothyronine 5'-monodeiodinase

T3



3,5,3'-triiodothyronine

Correlations (n=28)	**T4**	**T3**	**T3/T4**
T3	-0.15, p=0.46	--	--
T3/T4	**-0.67**, p=0.0001	**0.56**, p=0.003	--
Deiodinase	**-0.69**, p=0.041	**0.55**, p=0.013	**0.94**, p=0.0001

Thyroxine (T4) Levels in Hornyhead Turbot

SOUTHERN CALIFORNIA