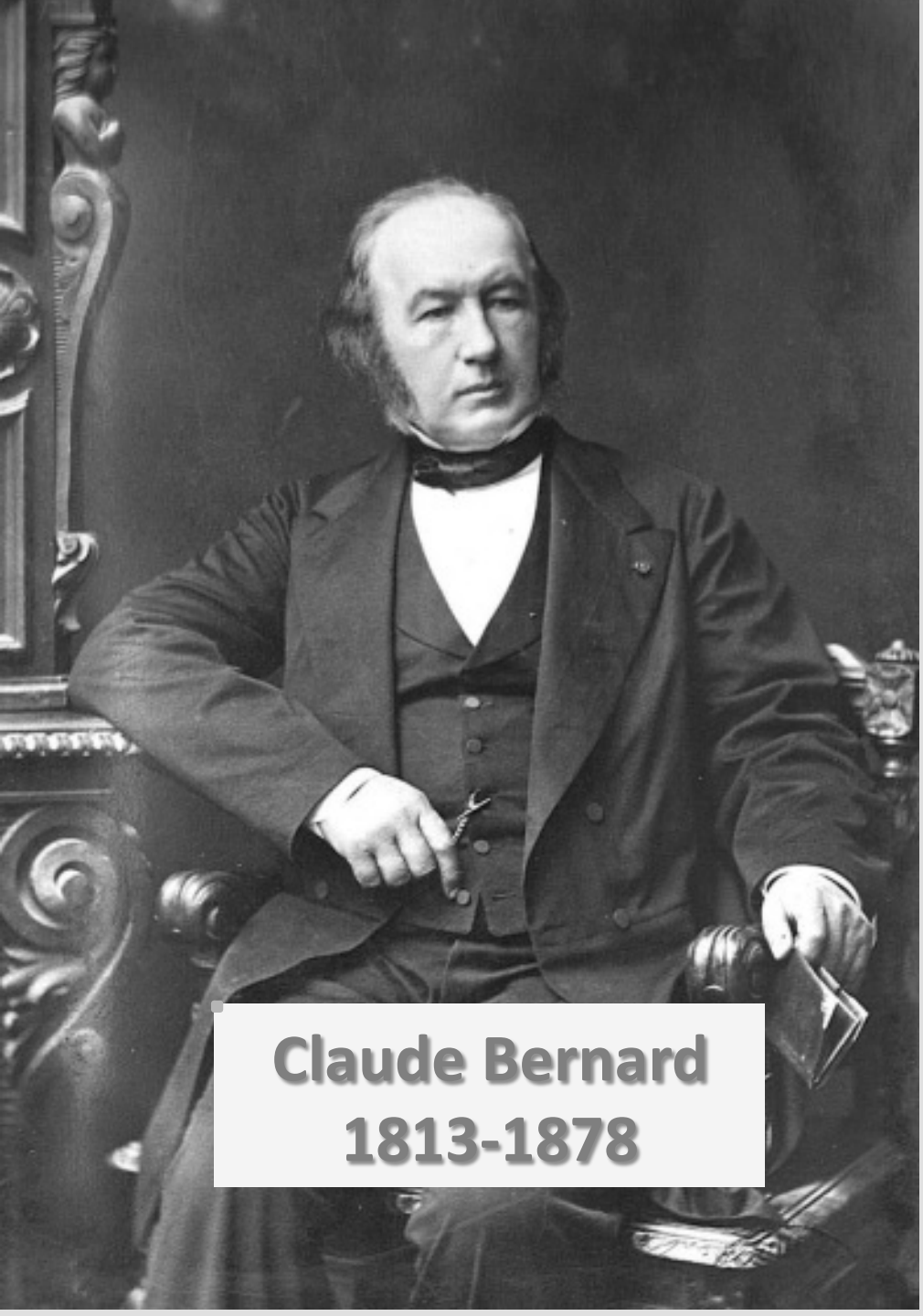
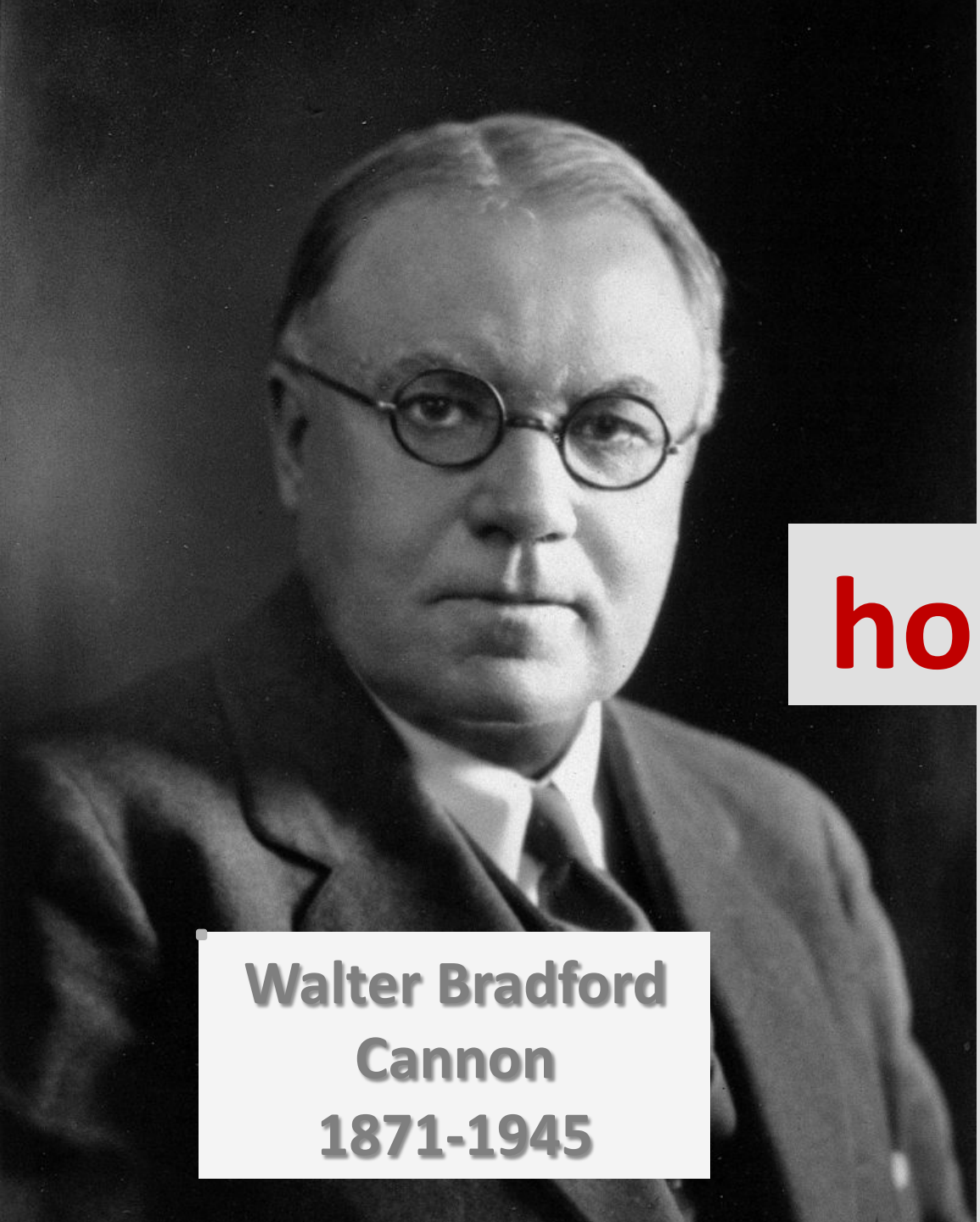
omeostasi endocrina

nel paziente oncologico

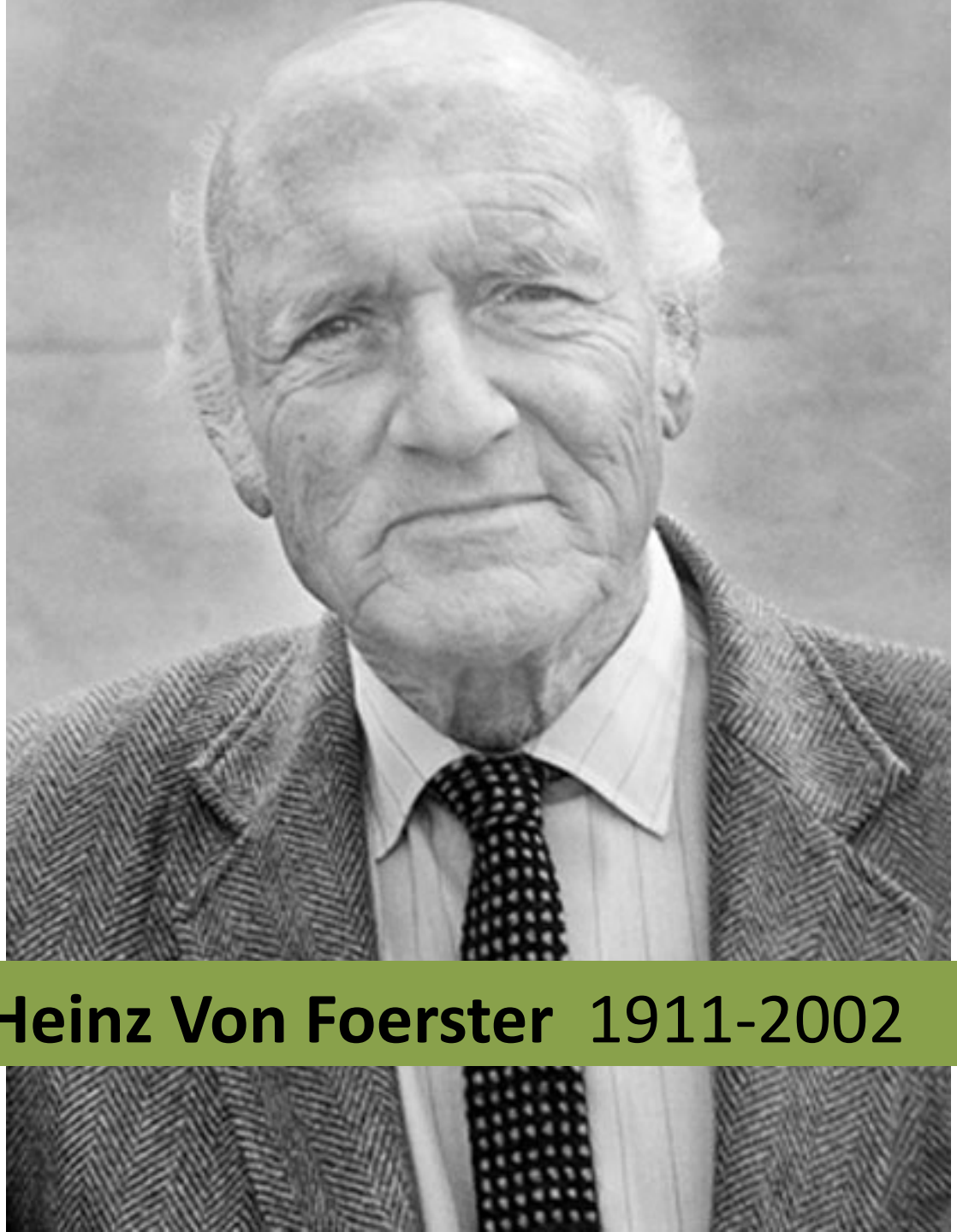


«fixité du milieu intérieur»



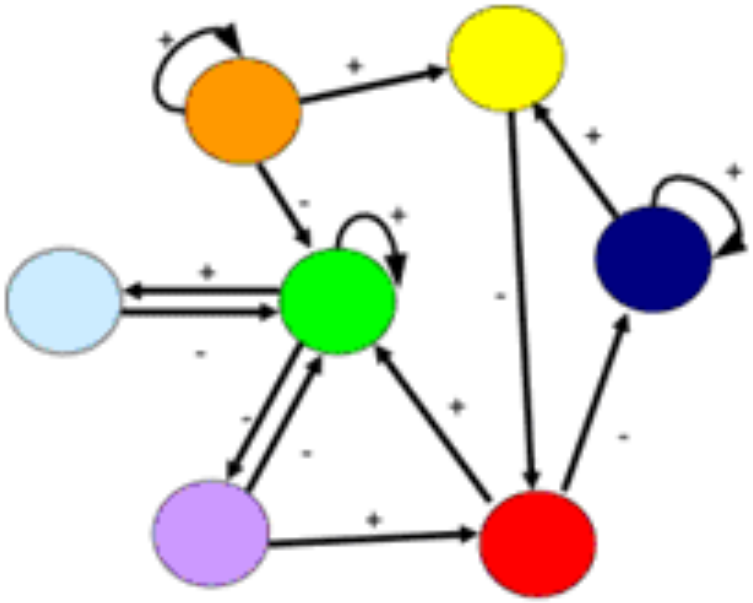
Walter Bradford Cannon
1871-1945

homeostasis

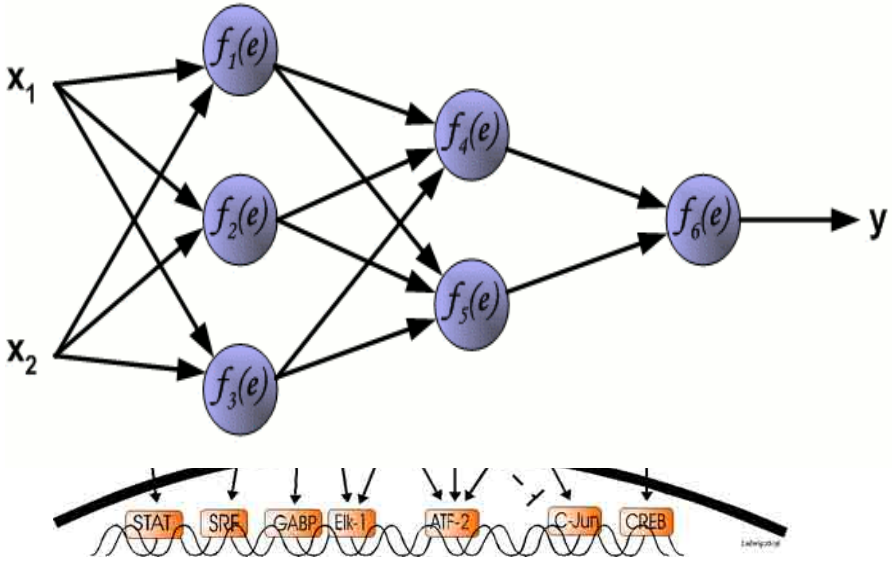


Heinz Von Foerster 1911-2002

complexity ≠ complication



Feedback in dynamic network models



omeoresi

mantenimento di equilibrio fluttuante

Jacques Monod
1910-1976

Francois Jacob
1920-2013

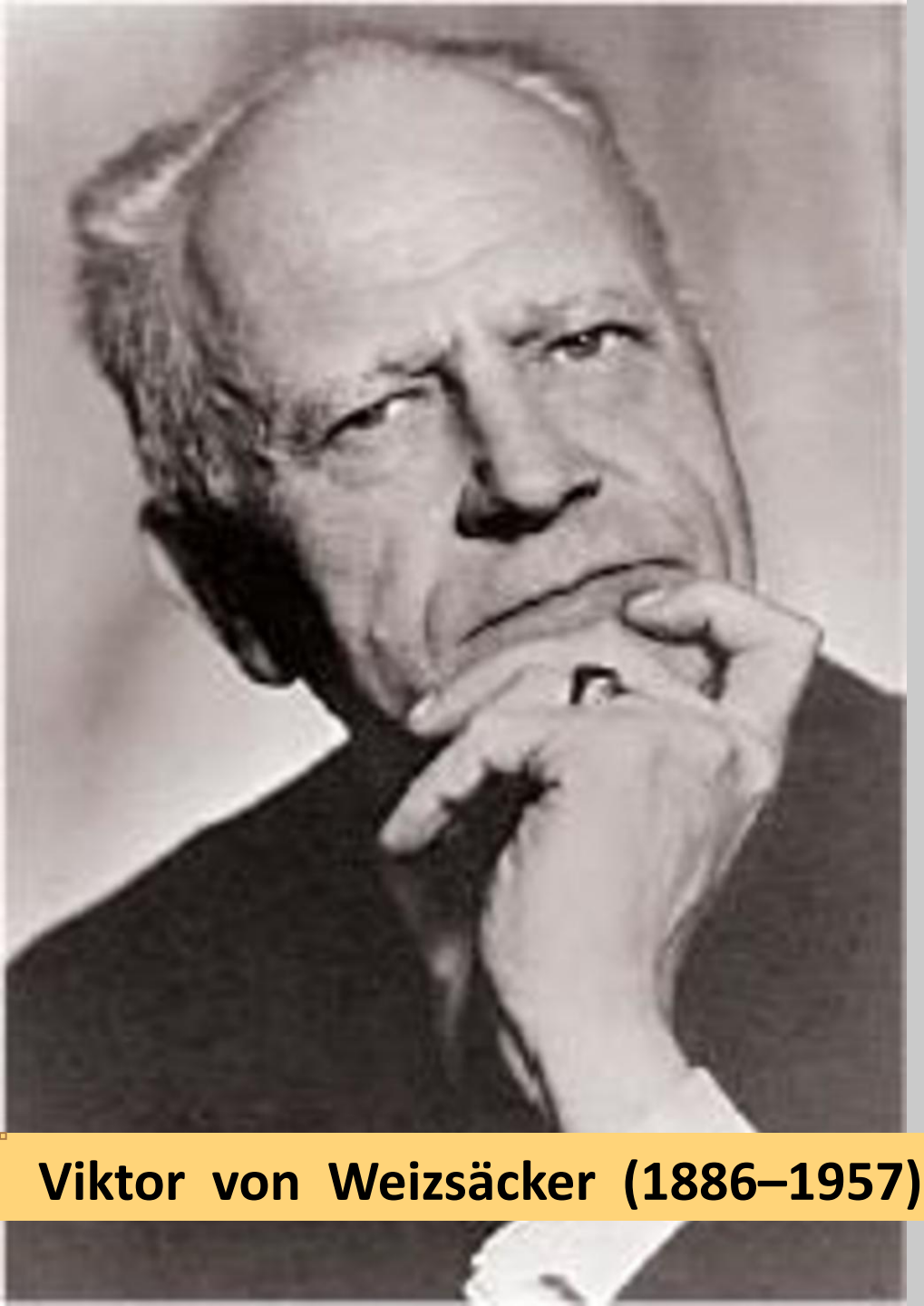
emergence

self-organisation

autopoiesys

far-from-equilibrium dynamics

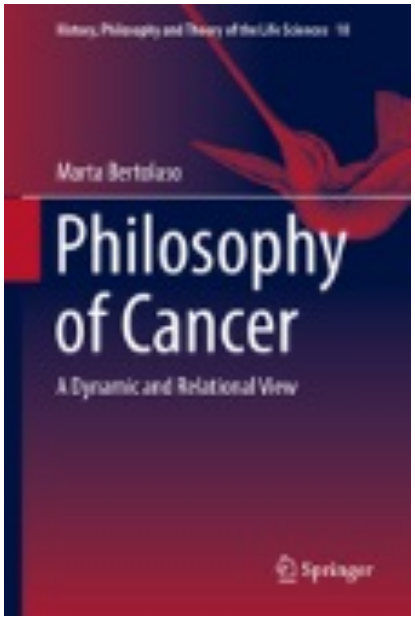
Stuart Kauffman 1939



Viktor von Weizsäcker (1886–1957)

funktionswandel

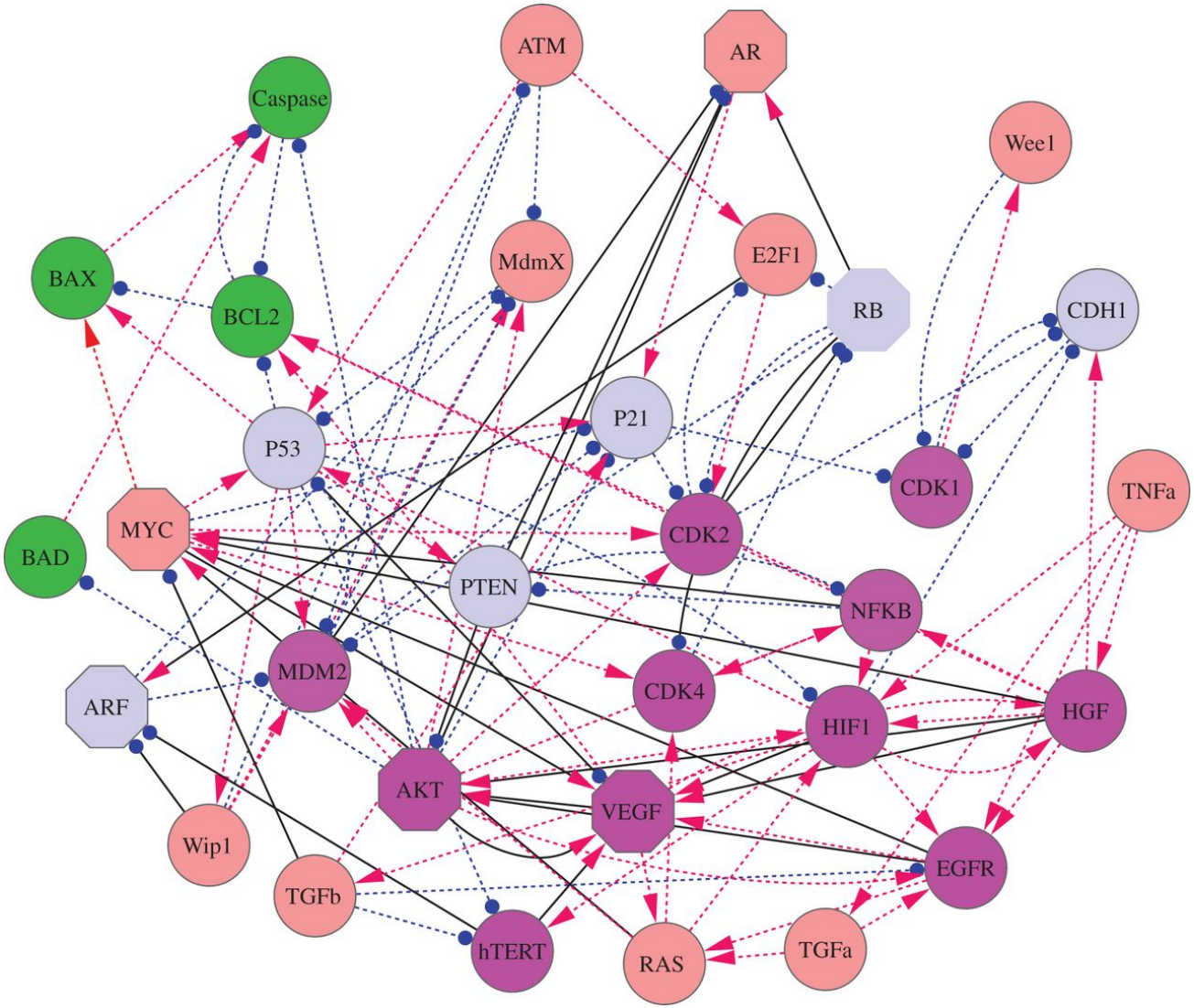

poiché l'essere vivente non è una cosa, la malattia che lo colpisce neppure lo può essere
Georges Canguilhem (1904-1995)


History, Philosophy and Theory of the Life Sciences 18
Marta Bertolaso
Philosophy of Cancer
A Dynamic and Relational View
Springer

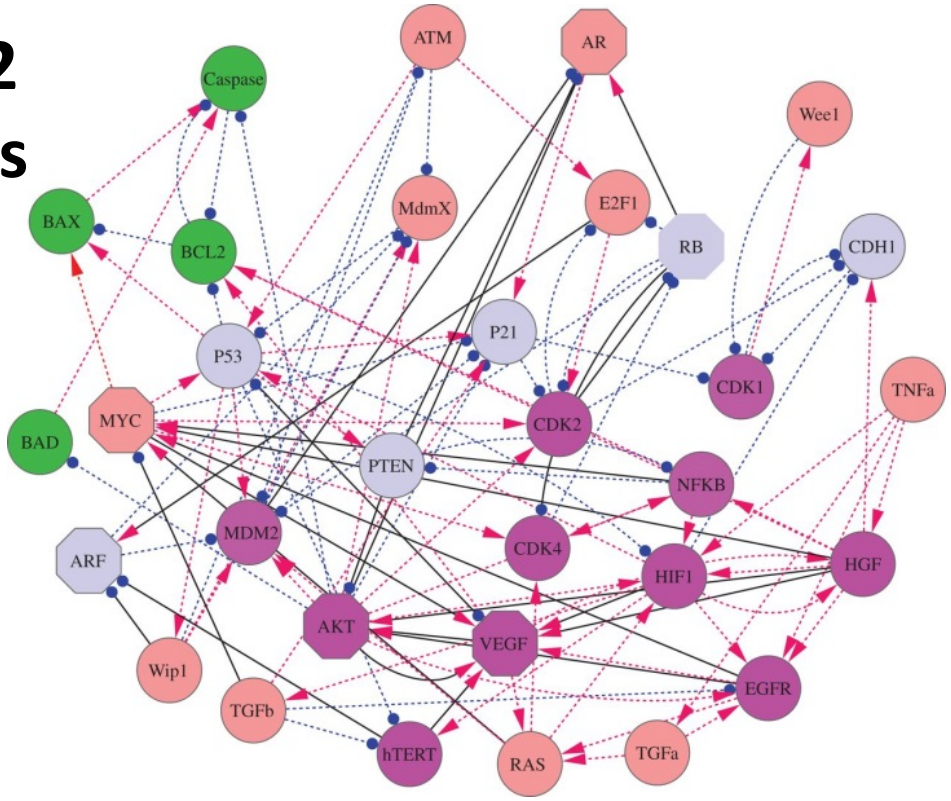
Quantifying the underlying landscape and paths of cancer

Chunhe Li, Jin Wang

Published 17 September 2014. DOI: 10.1098/rsif.2014.0774



cancer network including 32 nodes (genes) and 111 edges (66 activation interactions and 45 repression interactions).



red arrows: activation

blue filled circles: repression

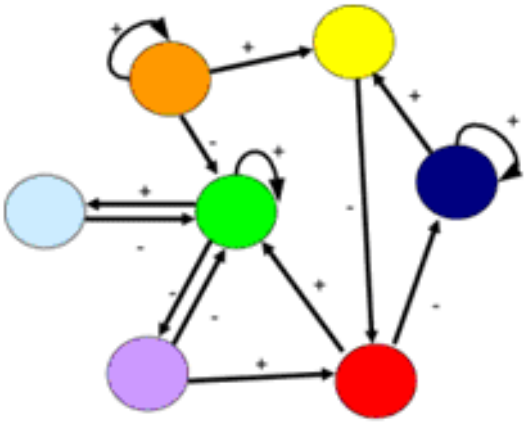
green nodes: apoptosis marker genes (BAX, BAD, BCL2, Caspase)

magenta nodes: cancer marker genes (AKT, MDM2, CDK2, CDK4, CDK1, NFKB, hTERT, VEGF, HIF1, HGF and EGFR)

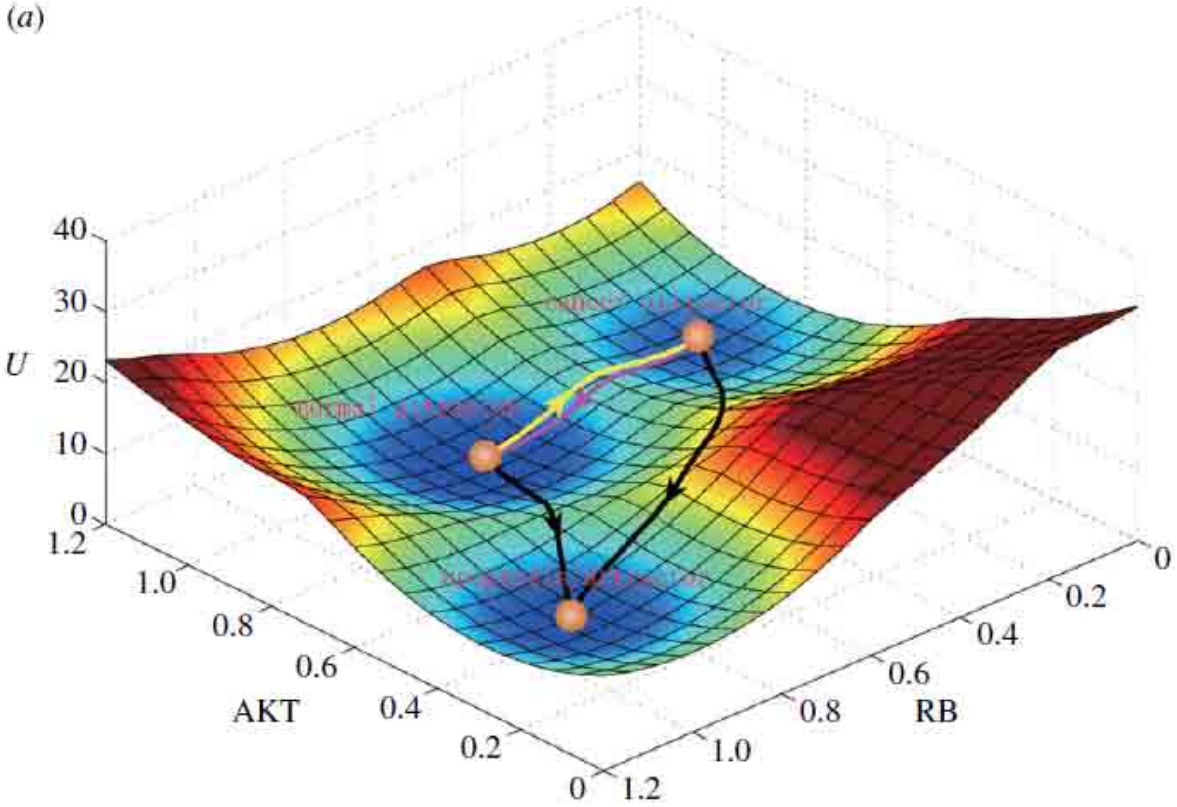
light blue nodes tumour repressor genes (P53, RB, P21, PTEN, ARF, CDH1)

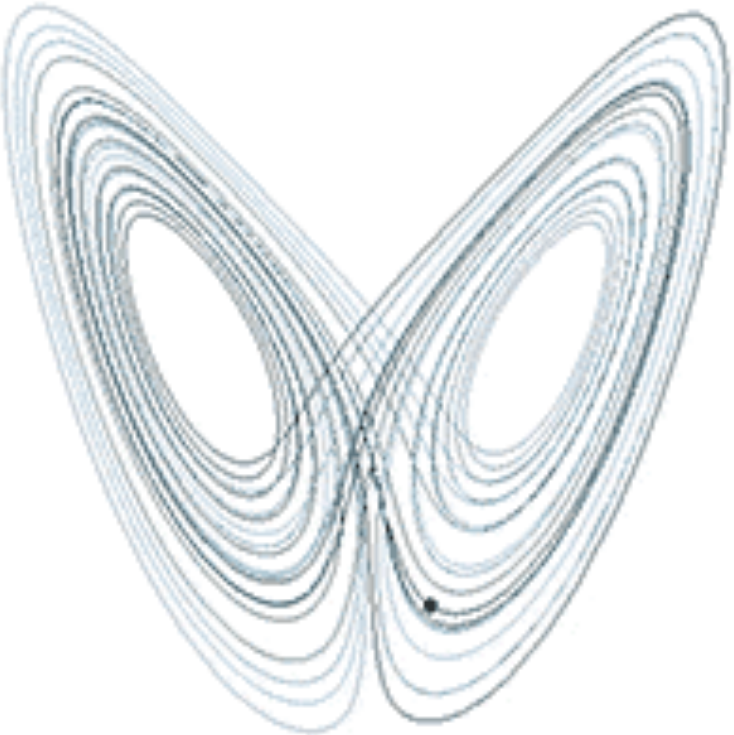
brown nodes represent other genes

octagon shape nodes represent key genes for the transition between normal and cancer states found by global sensitivity analysis



(*a*)





- **epidemiologia**

Short Communication

Cancer risk in patients hospitalised for Graves' disease: a population-based cohort study in Sweden

British Journal of Cancer (2010) 102, 1397 – 1399

X Shu[*,1,2], J Ji[2], X Li[2], J Sundquist[2,3], K Sundquist[1] and K Hemminki[1,2,4]

[1]Center for Family and Community Medicine, Karolinska Institute, 141 83 Huddinge, Sweden; [2]Center for Primary Health Care Research, Lund University, 205 02 Malmö, Sweden; [3]Stanford Prevention Research Center, Stanford University School of Medicine, Stanford, CA 5411, USA; [4]Division of Molecular Genetic Epidemiology, German Cancer Research Center (DKFZ), Im Neuenheimer Feld 580, D-69120 Heidelberg, Germany

Table 1 SIRs for subsequent cancers in patients hospitalised for Graves' disease by follow-up time

	Follow-up interval (years)																							
	<1				1–4				5–9				⩾10				All				All 1+			
Cancer site	**O**	**SIR**	**95% CI**		**O**	**SIR**	**95% CI**		**O**	**SIR**	**95% CI**		**O**	**SIR**	**95% CI**		**O**	**SIR**	**95% CI**		**O**	**SIR**	**95% CI**	
Upper aerodigestive tract	2	3.60	0.34	13.23	4	1.64	0.43	4.23	6	1.76	0.63	3.85	21	1.43	0.88	2.19	33	**1.56**	1.08	2.20	31	**1.51**	1.02	2.14
Stomach	2	3.43	0.32	12.62	0				7	1.76	0.70	3.64	15	0.73	0.41	1.20	24	0.86	0.55	1.28	22	0.81	0.51	1.22
Colon	0				8	0.78	0.33	1.55	11	0.75	0.37	1.34	59	0.81	0.61	1.04	78	**0.78**	0.61	0.97	78	**0.80**	0.63	0.99
Rectum	1	0.87	0.00	4.98	6	1.16	0.42	2.55	5	0.66	0.21	1.56	28	0.75	0.50	1.09	40	0.78	0.56	1.07	39	0.78	0.56	1.07
Liver	0				2	0.94	0.09	3.45	3	0.88	0.17	2.59	23	1.10	0.70	1.66	28	1.04	0.69	1.51	28	1.06	0.70	1.53
Pancreas	1	2.45	0.00	14.02	2	1.02	0.10	3.76	1	0.31	0.00	1.80	21	1.04	0.64	1.60	25	0.97	0.63	1.44	24	0.95	0.61	1.41
Lung	2	1.57	0.15	5.77	13	**2.14**	1.13	3.66	13	1.34	0.71	2.29	60	1.05	0.80	1.35	88	1.19	0.95	1.46	86	1.18	0.94	1.46
Breast	15	1.61	0.90	2.67	49	1.19	0.88	1.57	69	1.20	0.94	1.52	259	1.09	0.96	1.24	392	**1.14**	1.03	1.26	377	**1.12**	1.01	1.24
Cervix	1	0.70	0.00	4.01	3	0.53	0.10	1.57	9	1.39	0.63	2.65	13	0.81	0.43	1.39	26	0.88	0.57	1.29	25	0.89	0.57	1.31
Endometrium	2	1.01	0.10	3.73	7	0.82	0.33	1.70	21	**1.83**	1.13	2.79	41	0.81	0.58	1.09	71	0.97	0.76	1.23	69	0.97	0.76	1.23
Ovary	1	0.73	0.00	4.17	3	0.50	0.10	1.49	6	0.75	0.27	1.64	32	0.96	0.66	1.36	42	0.86	0.62	1.17	41	0.87	0.62	1.18
Prostate	2	1.18	0.11	4.33	7	0.88	0.35	1.83	10	0.79	0.38	1.46	63	0.95	0.73	1.21	82	0.92	0.73	1.15	80	0.92	0.73	1.14
Kidney	2	2.89	0.27	10.61	6	1.95	0.70	4.27	5	1.15	0.36	2.69	21	1.02	0.63	1.56	34	1.18	0.82	1.66	32	1.14	0.78	1.61
Urinary bladder	2	1.76	0.17	6.49	11	**2.19**	1.09	3.93	8	1.11	0.48	2.20	37	1.12	0.79	1.55	58	1.25	0.95	1.62	56	1.24	0.94	1.61
Melanoma	4	2.13	0.55	5.50	4	0.50	0.13	1.29	14	1.34	0.73	2.25	19	**0.53**	0.32	0.82	41	**0.73**	0.52	0.99	37	**0.68**	0.48	0.94
Skin	0				4	0.71	0.18	1.83	11	1.32	0.66	2.37	29	0.70	0.47	1.01	44	0.78	0.57	1.05	44	0.80	0.58	1.07
Nervous system	8	**6.57**	2.81	13.01	6	1.14	0.41	2.50	4	0.57	0.15	1.48	24	0.90	0.58	1.35	42	1.05	0.76	1.42	34	0.88	0.61	1.23
Thyroid gland	145	**234.07**	197.52	275.47	10	**4.04**	1.93	7.46	2	0.70	0.07	2.58	7	0.92	0.36	1.90	164	**12.08**	10.30	14.07	19	1.47	0.88	2.29
Endocrine glands	44	**42.17**	30.63	56.64	7	1.57	0.62	3.25	8	1.37	0.58	2.71	12	0.57	0.29	1.00	71	**2.20**	1.71	2.77	27	0.86	0.57	1.26
Parathyroid	42	***50.80***	36.60	68.71	5	1.45	0.46	3.42	5	1.14	0.36	2.68	10	0.65	0.31	1.20	62	**2.55**	1.96	3.27	20	0.86	0.53	1.33
Non-Hodgkin's lymphoma	1	1.09	0.00	6.25	2	0.48	0.05	1.78	5	0.83	0.26	1.95	18	**0.62**	0.36	0.98	26	**0.64**	0.42	0.95	25	**0.63**	0.41	0.94
Leukaemia	0				1	0.31	0.00	1.76	4	0.84	0.22	2.18	22	0.96	0.60	1.45	27	0.85	0.56	1.24	27	0.87	0.57	1.27
All	236	**6.96**	6.10	7.91	162	1.08	0.92	1.26	233	1.11	0.97	1.26	864	**0.93**	0.87	0.99	1495	**1.13**	1.07	1.19	1259	0.97	0.92	1.03

Abbreviations: O = observed; SIR = standardised incidence ratio; CI = confidence interval. Bold type, 95% CI does not include 1.00; bold type with underline, 99% CI does not include 1.00.

Hypothyroidism and hyperthyroidism and

Table 2 Standardized incidence ratios for breast cancer in women with hypothyroidism and hyperthyroidism, Denmark, 1978–2013.

	Women with hypothyroidism			Women with hyperthyroidism		
	No. of person-years	Observed/ expected cancer	SIR (95% CI)	No. of person-years	Observed/ expected cancer	SIR (95% CI)
Overall	36 1640	970/1031	0.94 (0.88–1.00)	674 236	2122/1903	1.11 (1.07–1.16)
Age at diagnosis of thyroid disease						
<30 years	37 559	17/15	1.17 (0.68–1.88)	72 244	35/45	0.78 (0.54–1.08)
30–49 years	102 422	197/206	0.96 (0.83–1.10)	229 087	626/510	1.23 (1.13–1.33)
50–69 years	137 188	486/505	0.96 (0.88–1.05)	255 053	1004/922	1.09 (1.02–1.16)
≥70 years	84 472	270/306	0.88 (0.78–0.99)	117 852	457/426	1.07 (0.98–1.18)
Calendar period of the diagnosis of thyroid disease						
1978–1982	35 984	95/95	1.00 (0.81–1.23)	111 722	309/288	1.07 (0.96–1.20)
1983–1987	3292	79/92	0.85 (0.68–1.06)	79 651	250/215	1.17 (1.03–1.32)
1988–1992	41 069	145/122	1.19 (1.00–1.40)	77 714	249/220	1.13 (0.99–1.28)
1993–1997	63 914	181/188	0.96 (0.83–1.11)	139 540	475/403	1.18 (1.08–1.29)
1998–2002	76 474	194/223	0.87 (0.75–1.00)	141 060	448/415	1.08 (0.98–1.18)
2003–2007	76 232	191/221	0.87 (0.75–1.00)	96 007	302/283	1.07 (0.95–1.19)
2008–2013	35 045	85/89	0.95 (0.76–1.18)	28 542	89/79	1.12 (0.90–1.38)
Charlson comorbidity index score						
Low (0)	273 988	706/746	0.95 (0.88–1.02)	57 3498	1734/1563	1.11 (1.06–1.16)
Moderate (1–2)	75 678	217/242	0.90 (0.78–1.02)	89 699	346/300	1.16 (1.04–1.28)
High (≥3)	11 974	47/42	1.12 (0.82–1.49)	11 038	42/40	1.04 (0.75–1.41)
Obesity diagnosis						
No	337 465	918/963	0.95 (0.89–1.02)	659 357	2075/1860	1.12 (1.07–1.16)
Yes	24 175	52/68	0.77 (0.57–1.01)	14 878	47/44	1.08 (0.79–1.43)
Alcohol-related disease						
No	354 797	943/1010	0.93 (0.88–1.00)	668 539	2106/1888	1.12 (1.07–1.16)
Yes	6842	27/21	1.30 (0.86–1.89)	5697	16/15	1.05 (0.60–1.71)
Breast cancer stage at diagnosis						
Localized	361 640	467/491	0.95 (0.87–1.04)	674 236	1012/909	1.11 (1.05–1.18)
Non-localized	361 640	377/427	0.88 (0.80–0.98)	674 236	883/809	1.09 (1.02–1.17)
Unknown stage	361 640	126/113	1.11 (0.93–1.32)	674 236	227/185	1.23 (1.07–1.40)
ER status[a]						
ER negative	200 431	67/77	0.87 (0.67–1.10)	293 504	124/118	1.05 (0.88–1.26)
ER positive	200 431	387/423	0.91 (0.83–1.01)	293 504	701/637	1.10 (1.02–1.19)
Missing ER status	200 431	55/70	0.78 (0.59–1.02)	293 504	100/103	0.97 (0.79–1.18)
Length of follow-up						
1–5 years	161 183	390/424	0.92 (0.83–1.02)	244 231	661/615	1.07 (0.99–1.16)
>5 years	200 457	580/607	0.96 (0.88–1.04)	430 005	1461/1288	1.13 (1.08–1.19)

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409–414

Cancer Risk in Patients with Graves' Disease: A Nationwide Cohort Study

THYROID
Volume 23, Number 7, 2013

DOI: 10.1089/thy.2012.0568

Yen-Kung Chen,[1–3] Cheng-Li Lin,[4] Yen-Jung Chang,[4] Fiona Tsui-Fen Cheng,[5,6] Chiao-Ling Peng,[4] Fung-Chang Sung,[7] Ya-Hsin Cheng,[8] and Chia-Hung Kao[8]

TABLE 3. SITE-SPECIFIC INCIDENCE RATE RATIO AND HAZARD RATIOS OF CANCER BETWEEN PATIENTS WITH AND WITHOUT GRAVES' DISEASE

	Graves' disease					
	Without		*With*			
Cancer (ICD-9-CM code)	*Event*	*Rate*[a]	*Event*	*Rate*[a]	*IRR [CI]*	*Adjusted HR*[b] *[CI]*
Head and neck (140–149)	22	0.17	8	0.25	1.44 (1.30, 1.61)***	1.28 (0.56, 2.89)
Stomach (151)	21	0.16	5	0.16	0.95 (0.83, 1.07)	0.94 (0.35, 2.51)
Colon (153, 154)	59	0.46	9	0.28	0.61 (0.53, 0.69)***	0.61 (0.30, 1.24)
Hepatoma (155)	42	0.33	13	0.40	1.23 (1.10, 1.37)**	1.13 (0.60, 2.12)
Lung (162)	42	0.33	7	0.22	0.66 (0.58, 0.75)***	0.69 (0.31, 1.54)
Breast (174)	97	0.76	39	1.21	1.60 (1.46, 1.75)***	1.58 (1.09, 2.30)*
Uterus (179, 182)	15	0.12	2	0.06	0.53 (0.45, 0.62)***	0.50 (0.11, 2.19)
Cervical (180)	30	0.24	3	0.09	0.40 (0.34, 0.47)***	0.45 (0.14, 1.47)
Ovary (183)	14	0.11	0	0.00	—	—
Prostate (185)	5	0.04	3	0.09	2.38 (2.14, 2.65)***	1.97 (0.45, 8.54)
Bladder (188)	14	0.11	3	0.09	0.85 (0.75, 0.97)*	0.81 (0.23, 2.84)
Kidney (189)	18	0.14	5	0.16	1.10 (0.98, 1.24)	1.00 (0.37, 2.72)
Thyroid (193)	20	0.16	52	1.62	10.3 (9.31, 11.5)***	10.4 (6.18, 17.4)***
Hematologic (200–208)	25	0.20	3	0.09	0.48 (0.41, 0.56)***	0.48 (0.14, 1.59)
Others	33	0.26	6	0.19	0.72 (0.63, 0.82)***	0.70 (0.29, 1.67)

[a]Incidence rate (per 1000 person-years).
[b]Multivariable analysis including sex, age, and comorbidities of diabetes, hypertension, and hyperlipidemia.
*$p<0.05$; **$p<0.01$; ***$p<0.001$.

- **epidemiologia**
- **possibili meccanismi di danno**

Thyroid hormone and anti-apoptosis in tumor cells

Hung-Yun Lin[1,2], Gennadi V. Glinsky[3], Shaker A. Mousa[4], Paul J. Davis[4,5]

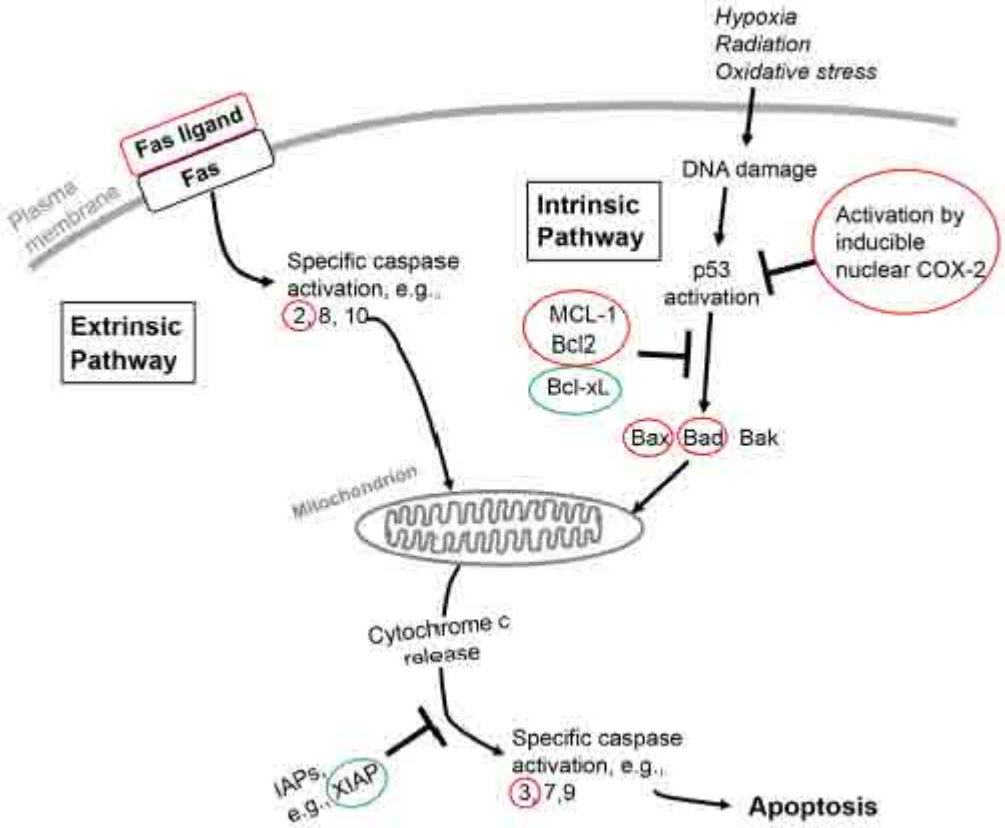
[1]PhD Program for Cancer Biology and Drug Discovery, College of Medical Science and Technology, Taipei, Taiwan

[2]Taipei Cancer Center, Taipei Medical University, Taipei, Taiwan

[3]Stanford University, Palo Alto, CA, USA

[4]Pharmaceutical Research Institute, Albany College of Pharmacy and Health Sciences, Albany, NY, USA

[5]Department of Medicine, Albany Medical College, Albany, NY, USA



- **Epidemiologia**
- **meccanismi lineari**
- **clinica**

The Oncologist®

Symptom Management and Supportive Care

Medically Induced Euthyroid Hypothyroxinemia May Extend Survival in Compassionate Need Cancer Patients: An Observational Study

ALECK HERCBERGS,[a] REBECCA E. JOHNSON,[b] OSNAT ASHUR-FABIAN,[c] DAVID H. GARFIELD,[d,e] PAUL J. DAVIS[f,g]

The Oncologist 2015;20:72–76

the difference between actual and expected survival was significant at the p <.01 level in comparisons of the total population

ORIGINAL ARTICLE

Association Between Development of Hypothyroidism and Improved Survival in Patients With Head and Neck Cancer

Marc Nelson, MD; Alech Herchergs, MD; Lisa Rybicki, MS; Marshall Strome, MD

Arch Otolaryngol Head Neck Surg. 2006;132:1041-1046

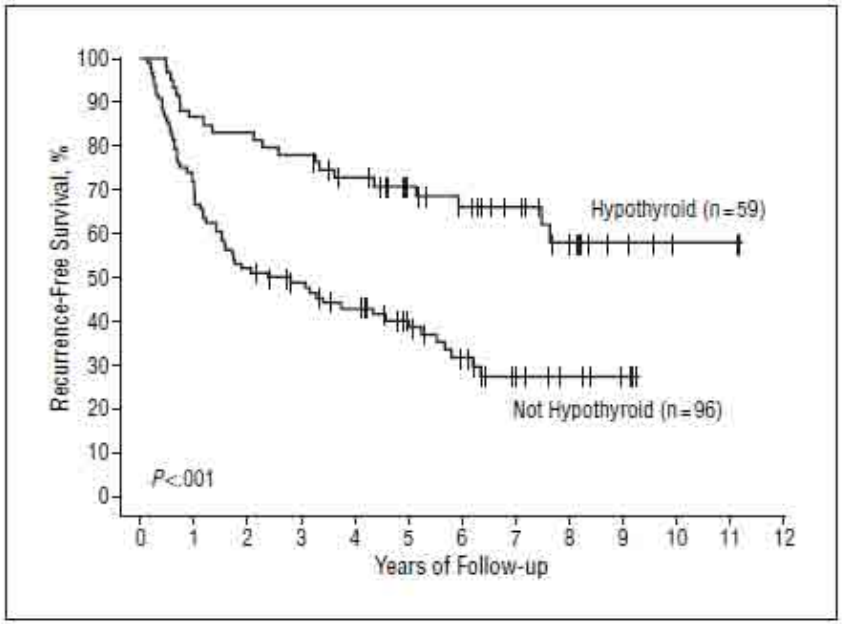


Figure 1. Unadjusted Kaplan-Meier recurrence-free survival analysis.

	Recurrence		Death		Recurrence or Death	
Variable	HR (95% CI)	*P* Value	HR (95% CI)	*P* Value	HR (95% CI)	*P* Value
Unadjusted Analyses						
Hypothyroid, all patients (N = 155)						
Yes/No	0.49 (0.28-0.88)	.02	0.30 (0.17-0.52)	<.001	0.37 (0.22-0.61)	<.001

- epidemiologia
- meccanismi lineari
- clinica
- strategie

REVIEW

Complexity in the signaling network: insights from the use of targeted inhibitors in cancer therapy

Jeremy S. Logue and Deborah K. Morrison[1]

Laboratory of Cell and Developmental Signaling, National Cancer Institute at Frederick, Frederick, Maryland 21702, USA

GENES & DEVELOPMENT 2012 26:641–650

Cancer cells respond to chronic drug treatment by adapting their signaling circuitry, taking advantage of pathway redundancy and routes of feedback and cross-talk to maintain their function.

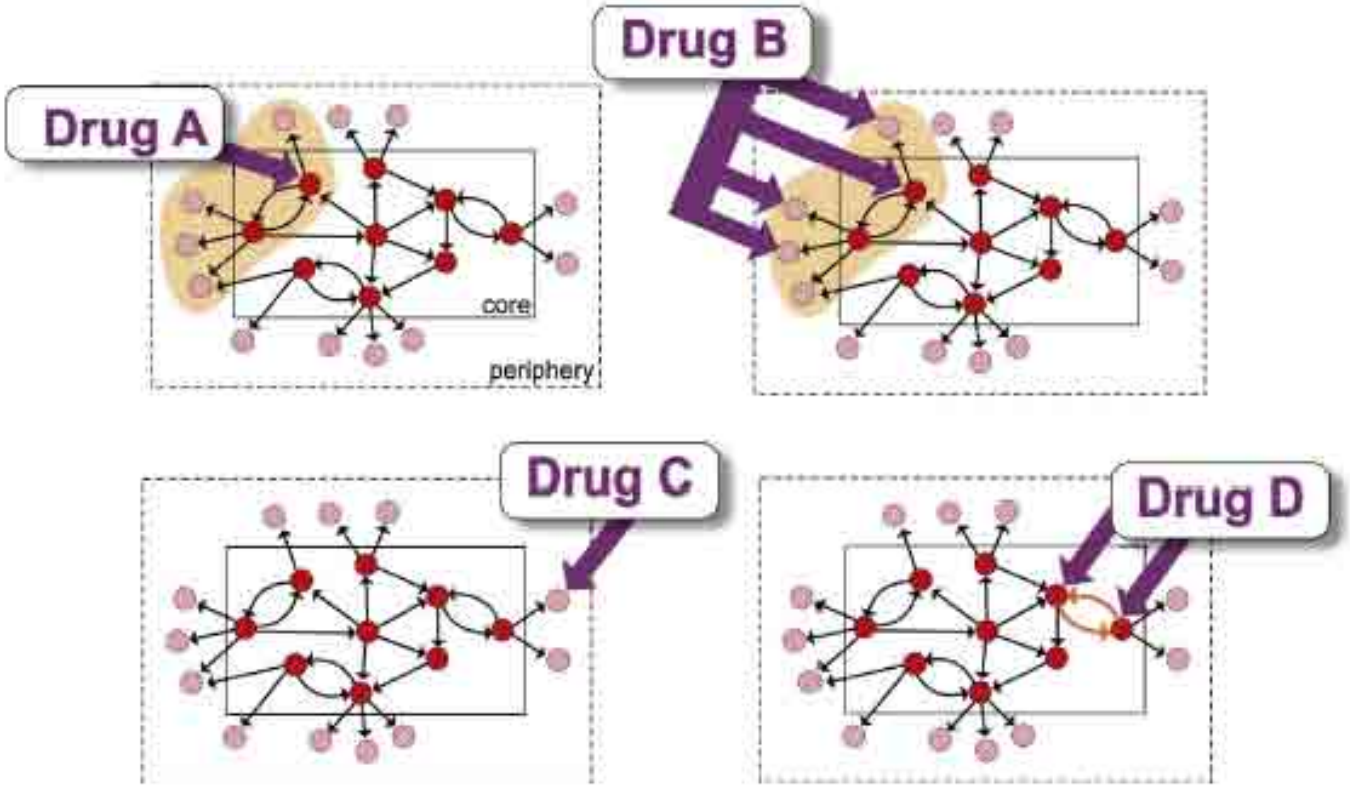
Review

How to escape the cancer attractor: Rationale and limitations of multi-target drugs

Seminars in Cancer Biology 23 (2013) 270–278

Sui Huang[a,b,*], Stuart Kauffman[b,c]

[a] Institute for Systems Biology, Seattle WA, United States
[b] Institute for Biocomplexity and Informatics, University of Calgary, Canada
[c] College of Medicine, Biochemistry & CEMS, Department of Mathematics & Statistics, University of Vermont, United States



Sunitinib-induced hypothyroidism predicts progression-free survival in metastatic renal cell carcinoma patients

Anna Buda-Nowak[1] · Jakub Kucharz[2,3] · Paulina Dumnicka[4] · Marek Kuzniewski[5] · Roman Maria Herman[2] · Aneta L. Zygulska[1] · Beata Kusnierz-Cabala[6]

Med Oncol (2017) 34:68

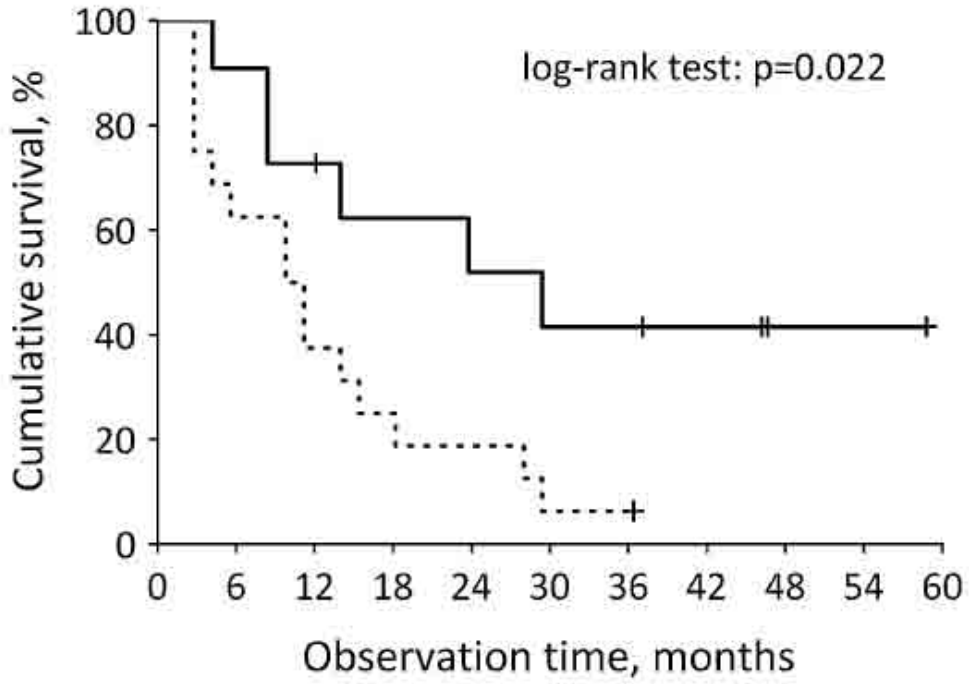
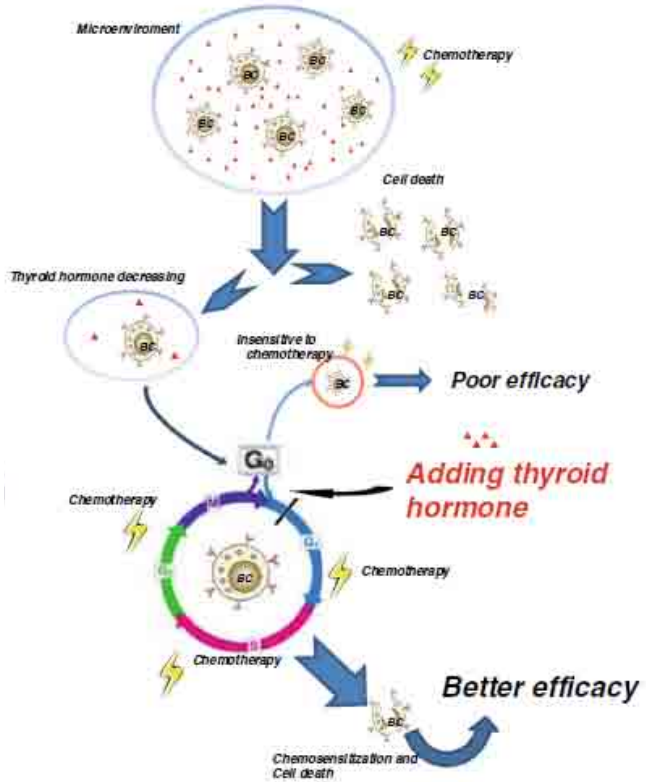


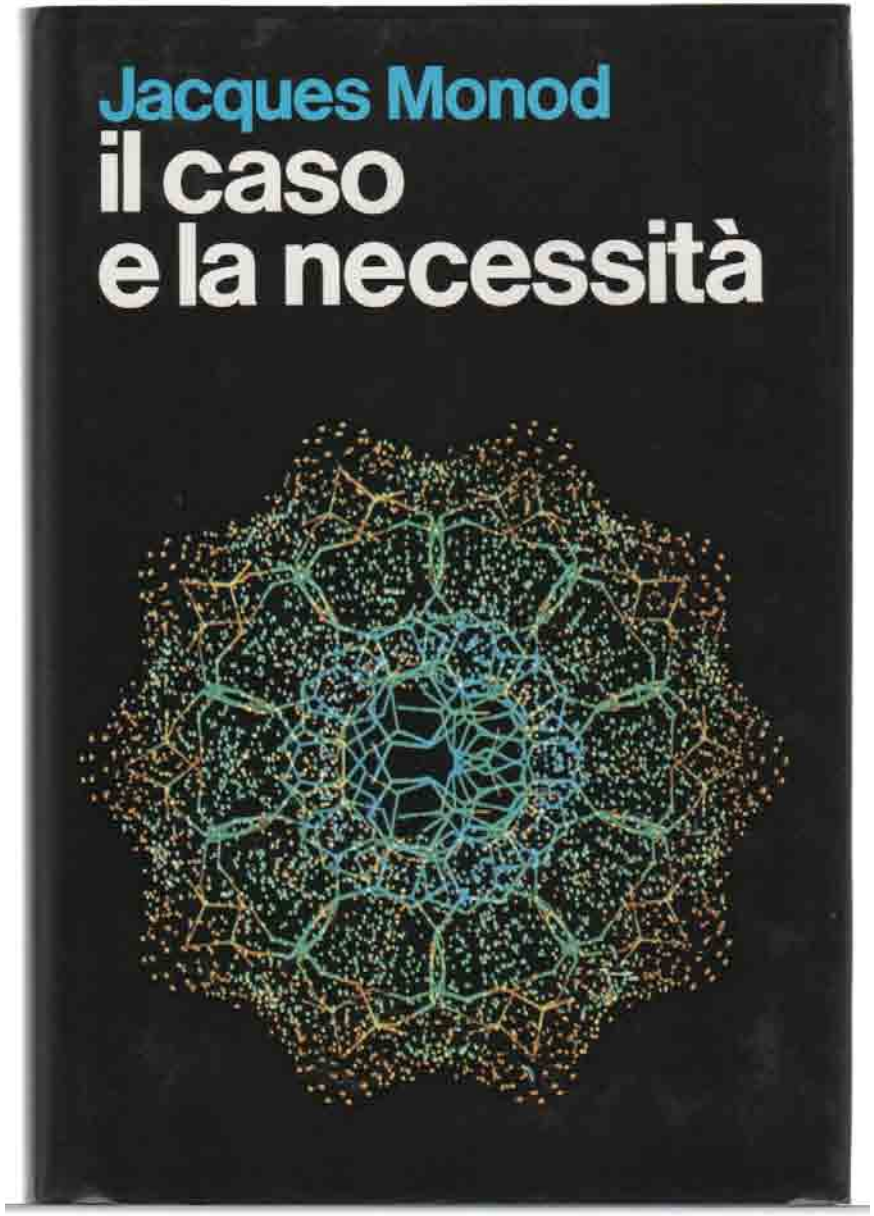
Fig. 1 Cumulative survival in patients who developed hypothyroidism during sunitinib treatment (*solid line*) and those who did not (*dashed line*)

Implication from thyroid function decreasing during chemotherapy in breast cancer patients: chemosensitization role of triiodothyronine

Jianbo Huang, Liangbin Jin†, Guangyan Ji, Lei Xing†, Chaobo Xu, Xiong Xiong, Hongyuan Li, Kainan Wu, Guosheng Ren* and Lingquan Kong*

Huang *et al. BMC Cancer* 2013, **13**:334
http://www.biomedcentral.com/1471-2407/13/334




Jacques Monod
il caso
e la necessità


Prefazione di Mario Rasetti
STUART KAUFFMAN
Reinventare il sacro
codice
EDIZIONI

Le cose sono unite da legami invisibili: non si può cogliere un fiore senza turbare una stella