APPENDIX

TABLE 1: **Comparison between the real incidence of cancer observed in 42 species of mammals and the cancer incidence predicted by assuming either the individual cell or the organ as the unit of carcinogenesis**

				Incidence of cancer per individual per lifespan			
				Real	Predicted		
					Assuming that the unit of carcinogenesis is:		
					The individual cell		The organ (or part of it)
Species	Body size	Lifespan	ms-BMR referred to mouse		All cells are equivalent	Cells with ≠ msBMR	All cells are equivalent	Cells with ≠ msBMR
Mouse	30 g	2 y	1	0.25	0.25	0.25	0.25	0.25
N.mole rat*	35 g	30 y	0.67	0.02	4.38	2.9	3.75	2.51
Marmoset	260 g	8 y	0.49	0.12	13	6.4	1.00	0.49
Rat	280 g	3 y	0.51	0.21	3.5	1.8	0.38	0.19
Squirrel	430 g	3 y	0.61	0.17	5.4	3.3	0.38	0.23
Prairie dog	1.1 kg	5 y	0.24	0.21	23	6.5	0.63	0.15
Ferret	1.4 kg	8 y	0.36	0.36	47	16.9	1.00	0.36
Cat	4 kg	9 y	0.26	0.23	150	39.0	1.13	0.29
Rabbit	4 kg	10 y	0.28	0.30	167	46.8	1.25	0.35
Racoon	6 kg	3 y	0.31	0.13	75	23.3	0.38	0.12
Tasm. Devil**	7 kg	5 y	0.16	0.51	146	23.3	0.63	0.10
Rhesus m.	7 kg	15 y	0.22	0.18	438	96.3	1.88	0.41
Dog	25 kg	12 y	0.16	0.36	1,250	200.0	1.50	0.24
Afr. w. dog	26 kg	10 y	0.14	0.17	1,083	151.6	1.25	0.18
Peccary	30 kg	15 y	0.13	0.26	1,875	243.8	1.88	0.24
Wolf	32 kg	10 y	0.17	0.27	1,333	226.6	1.25	0.21
Cheetah	50 kg	11 y	0.18	0.25	2,292	412.5	1.38	0.25
Dom. pig	50 kg	15 y	0.15	0.30	3,125	468.8	1.88	0.28

Capybara	55 kg	10 y	0.16	0.15	2,292	366.7	1.25	0.20
R. kangaroo	55 Kg	13 y	0.12	0.15	2,979	357.5	1.63	0.20
Leopard	55 kg	15 y	0.18	0.35	3,438	618.8	1.88	0.34
Cougar	60 kg	15 y	0.16	0.33	3,750	600.0	1.88	0.30
Human*	70 kg	75 y	0.12	0.40	23,333	2,800.0	9.38	1.13
Dom. Goat	80 kg	11 y	0.12	0.07	5,667	680.0	1.38	0.17
Sheep	90 kg	11 y	0.12	0.20	4,125	495.0	1.38	0.17
Jaguar	100 kg	18 y	0.13	0.41	7,500	975.0	2.25	0.29
Harbor seal	115 kg	28 y	0.20	0.20	13,417	2,683.4	3.50	0.70
Llama	140 kg	15 y	0.15	0.11	8,750	1,312.5	1.88	0.28
Tiger	175 kg	23 y	0.11	0.34	16,771	1,844.8	2.88	0.32
Lion	175 kg	20 y	0.11	0.18	14,583	1,604.2	2.50	0.28
Sea lion	200 kg	15 y	0.16	0.22	12,500	2,000.0	1.88	0.30
Bear	300 kg	21 y	0.09	0.26	26,250	2,362.5	2.63	0.24
B. Dolphin	400 kg	35 y	0.12	0.11	58,333	7,000.0	4.38	0.53
Moose	460 kg	17 y	0.10	0.12	32,583	3,258.3	2.13	0.21
Horse	500 kg	25 y	0.08	0.17	58,333	4,666.6	3.13	0.25
Camel	550 kg	22 y	0.05	0.14	50,417	2,520.9	2.75	0.14
Bovine	650 kg	20 y	0.10	0.16	54,167	5,416.7	2,50	0.25
Bel. Whale	1.15 Ton	75 y	0.06	0.27	359,375	21,562.5	9.38	0.56
Rhinoceros	2 Ton	45 y	0.06	0.27	375,000	22,500.0	5.6	0.34
Elephant *	4.5 Ton	60 y	0.07	0.04	1,312,500	91,875.0	7.5	0.53
Bw. Whale*	80 Ton	160 y	0.028	< 0.01	53,333.333	1,493,333.3	20.00	0.56
Bl. Whale*	100 ton	80 y	0.025	≤ 0.05	33,333,333	833,333.3	10.00	0.25

Data for each species were obtained from three or more independents surveys carried out in animals in captivity or in wildlife; these surveys have been quoted in the text. For simplicity, only mean values were registered; in most cases standard error was 25% or lower of the mean value. Body mass and lifespan were obtained as mean of the different surveys for each species. When these data were not available, body mass and lifespan as well as mass-specific basal

metabolic rates (msBMR) were obtained from an Age Database (de Magalhaes et al, 2009); msBMR is the rate of energy expenditure per unit time and unit mass and was expressed in W (watts)/g (gram); in the case that some data for msBMR were not available, we have calculated msBMR from other parameters of metabolism such as heart rate. msBMR of the mouse, that is the reference value has been considered as 0.00903 W/g. N. mole rat = naked mole rat; Squirrel: data from red and ground squirrels were pooled; Tasm. Devil = Tasmanian devil; Rhesus m. = Rhesus monkey or Rhesus macaque; Peccary includes data from both collared and chacoan peccaries; Wolf summarizes data from gray, red and maned wolves; Dom. pig = Domestic Pot-bellied pig; R. kangaroo = Red kangaroo; Dom. Goat = Domestic goat; Bear summarizes data from brown, polar and other bears; B. Dolphin = Bottlenose dolphin; Camel summarizes data from camels and dromedaries; Bel. Whale = Beluga whale; Rhinoceros includes data from white and indian rhinoceroses; Bw. Whale = Bowhead whale; Bl. Whale = Blue whale. Real incidence of cancer per individual per lifespan was calculated as the ratio between the number of cancer observed in each individual of each species that died and the total number of animals that died naturally (naturally meaning that they were not slaughtered, hunted or killed before cancer age was attained as may occur in animals that are used for consumption). In the practice, in most cases, this value was obtained as the ratio between the number of necropsied animals with cancer x the number of cancer per individual and the total number of necropsied animals. In general only one cancer is present in each individual. Predicted incidence of cancer assuming both the individual cell as the unit of carcinogenesis, and cells of different species having equal msBMR was calculated as [the ratio between the mass of the animal and the mass of the mouse] x [the ratio between the lifespan of the animal and the lifespan of the mouse] x [0.25 (the real cancer incidence in the mouse)]. Predicted incidence of cancer assuming the individual cell as the unit of carcinogenesis, and cells of different species displaying different msBMR was calculated multiplying the [previous value] by [the ratio between the msBMR of the animal and that of the mouse]. Predicted incidence of cancer assuming the organ (or part of it) as the unit of carcinogenesis, and cells of different species having equal msBMR was calculated as [the ratio between the lifespan of the animal and the lifespan of the mouse] x [0.25]. Predicted incidence of cancer assuming the organ (or part of it) as the unit of carcinogenesis and cells of different species having different msBMR was calculated multiplying [the previous value] by [the ratio between the msBMR of the animal and that of the mouse]. Cancer Incidence predicted assuming the individual cell as the unit of carcinogenesis (either considering cells of all species displaying similar or different msBMR) was strikingly higher ($p < 0.001$) than the real incidence, for all species tested. Cancer incidence predicted assuming the organ (or part of it) as the unit of carcinogenesis and cells of all species displaying similar msBMR, was not significantly different than the real incidence for 11 species (marmoset, rat, squirrel, ferret, cat, raccoon, Tasmanian devil, leopard, sea lion, bottlenose dolphin and moose) and moderately higher ($p < 0.05$ and $p < 0.01$) than the real incidence for the remaining species tested. Cancer incidence predicted assuming the organ (or part of it) as the unit of carcinogenesis and cells of all species displaying different msBMR, was not significantly different than the real incidence for most species tested; only for five species marked with * (naked mole rat, human, elephant, bowhead whale and blue whale), this predicted value was higher than the real incidence of cancer ($p < 0.05$ for human and blue whale; $p < 0.01$ for naked mole rat and elephant and $p < 0.001$ for bowhead whale)and only for one species, marked with ** (Tasmanian devil), this predicted value was lower ($p < 0.001$) than the real incidence of cancer.