

M2 放射線基礎

DNA損傷修復と・細胞死・組織の反応

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放射線から何を連想しますか？

- 1. レントゲンの検査
- 2. 放射線治療
- 3. 広島、長崎、原爆
- 4. 原子炉、原子力発電
- 5. ラドン温泉
- 6. 何か怖いもの
- 7. その他

今日の目的

放射線治療をしているときにそこで何が起きているのかを理解する。

放射線がどのようにして細胞に影響を及ぼすのかを理解する。

放射線に対して細胞や組織はどのように反応するのかを理解する。

分かりやすく話す

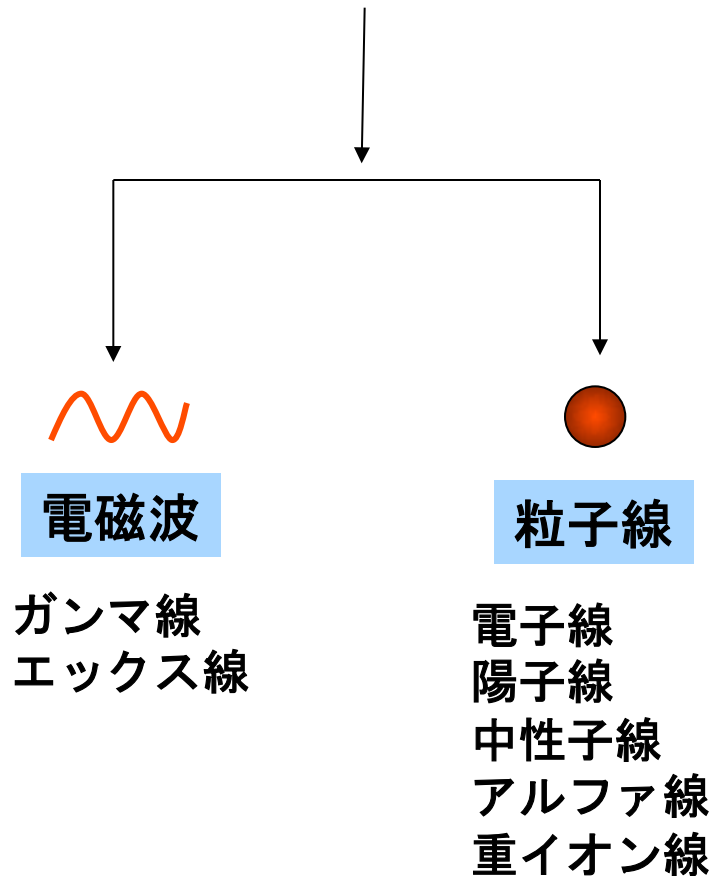
放射線とは何か？

エネルギーをもった電磁波または粒子

放射線の性質

- (1) 五感で感じられない。
見えない。音もしない。温度も感じない。匂いもしない。味もしない。
- (2) 物質を透過する。
骨や内部の構造が分かる。吸収の違いによる。
- (3) エネルギーを与えて変化を起こす
DNAに傷を作る→生物学的な影響を与える。
物質に傷を作る→物質の特性を変える。

放射線には、原子よりも小さな粒子線と
波長の短い光子線の2種類がある。



equipment, and to Dr. G. E. R. Deacon and the captain and officers of R.R.S. *Discovery II* for their part in making the observations.

¹ Young, F. B., Gerrard, H., and Jevons, W., *Phil. Mag.*, **40**, 149 (1920).

² Longuet-Higgins, M. S., *Mon. Not. Roy. Astron. Soc., Geophys. Supp.*, **5**, 285 (1949).

³ Von Arx, W. S., Woods Hole Papers in Phys. Oceanogr. Meteor., **11** (3) (1950).

⁴ Ekman, V. W., *Arkiv. Mat. Astron. Fysik. (Stockholm)*, **2** (11) (1905).

MOLECULAR STRUCTURE OF NUCLEIC ACIDS

A Structure for Deoxyribose Nucleic Acid

WE wish to suggest a structure for the salt of deoxyribose nucleic acid (D.N.A.). This structure has novel features which are of considerable biological interest.

A structure for nucleic acid has already been proposed by Pauling and Corey¹. They kindly made their manuscript available to us in advance of publication. Their model consists of three intertwined chains, with the phosphates near the fibre axis, and the bases on the outside. In our opinion, this structure is unsatisfactory for two reasons: (1) We believe that the material which gives the X-ray diagrams is the salt, not the free acid. Without the acidic hydrogen atoms it is not clear what forces would hold the structure together, especially as the negatively charged phosphates near the axis will repel each other. (2) Some of the van der Waals distances appear to be too small.

Another three-chain structure has also been suggested by Fraser (in the press). In his model the phosphates are on the outside and the bases on the inside, linked together by hydrogen bonds. This structure as described is rather ill-defined, and for this reason we shall not comment on it.

We wish to put forward a radically different structure for the salt of deoxyribose nucleic acid. This structure has two helical chains each coiled round the same axis (see diagram). We have made the usual chemical assumptions, namely, that each chain consists of phosphate diester groups joining β -D-deoxyribofuranose residues with 3',5' linkages. The two chains (but not their bases) are related by a dyad perpendicular to the fibre axis. Both chains follow right-handed helices, but owing to the dyad the sequences of the atoms in the two chains run in opposite directions. Each chain loosely resembles Furburg's² model No. 1; that is, the bases are on the inside of the helix and the phosphates on the outside. The configuration of the sugar and the atoms near it is close to Furburg's 'standard configuration', the sugar being roughly perpendicular to the attached base. There

is a residue on each chain every 3.4 Å, in the z-direction. We have assumed an angle of 36° between adjacent residues in the same chain, so that the structure repeats after 10 residues on each chain, that is, after 34 Å. The distance of a phosphorus atom from the fibre axis is 10 Å. As the phosphates are on the outside, cations have easy access to them.

The structure is an open one, and its water content is rather high. At lower water contents we would expect the bases to tilt so that the structure could become more compact.

The novel feature of the structure is the manner in which the two chains are held together by the purine and pyrimidine bases. The planes of the bases are perpendicular to the fibre axis. They are joined together in pairs, a single base from one chain being hydrogen-bonded to a single base from the other chain, so that the two lie side by side with identical z-co-ordinates. One of the pair must be a purine and the other a pyrimidine for bonding to occur. The hydrogen bonds are made as follows: purine position 1 to pyrimidine position 1; purine position 6 to pyrimidine position 6.

If it is assumed that the bases only occur in this structure in the most plausible tautomeric form (that is, with the keto rather than the enol configurations) it is found that only specific pairs of bases can bond together. These pairs are: adenine (purine) with thymine (pyrimidine), and guanine (purine) with cytosine (pyrimidine).

In other words, if an adenine forms one member of a pair, on either chain, then on these assumptions the other member must be thymine; similarly for guanine and cytosine. The sequence of bases on a single chain does not appear to be restricted in any way. However, if only specific pairs of bases can be formed, it follows that if the sequence of bases on one chain is given, then the sequence on the other chain is automatically determined.

It has been found experimentally^{3,4} that the ratio of the amounts of adenine to thymine, and the ratio of guanine to cytosine, are always very close to unity for deoxyribose nucleic acid.

It is probably impossible to build this structure with a ribose sugar in place of the deoxyribose, as the extra oxygen atom would make too close a van der Waals contact.

The previously published X-ray data^{5,6} on deoxyribose nucleic acid are insufficient for a rigorous test of our structure. So far as we can tell, it is roughly compatible with the experimental data, but it must be regarded as unproved until it has been checked against more exact results. Some of these are given in the following communications. We were not aware of the details of the results presented there when we devised our structure, which rests mainly though not entirely on published experimental data and stereochemical arguments.

It has not escaped our notice that the specific pairing we have postulated immediately suggests a possible copying mechanism for the genetic material.

Full details of the structure, including the conditions assumed in building it, together with a set of co-ordinates for the atoms, will be published elsewhere.

We are much indebted to Dr. Jerry Donohue for constant advice and criticism, especially on interatomic distances. We have also been stimulated by a knowledge of the general nature of the unpublished experimental results and ideas of Dr. M. H. J. Wilkins, Dr. R. E. Franklin and their co-workers at

King's College, London. One of us (J. D. W.) has been aided by a fellowship from the National Foundation for Infantile Paralysis.

J. D. WATSON
F. H. C. CRICK

Medical Research Council Unit for the Study of the Molecular Structure of Biological Systems, Cavendish Laboratory, Cambridge, April 2.

¹ Pauling, L., and Corey, R. B., *Nature*, **171**, 346 (1953); *Proc. U.S. Nat. Acad. Sci.*, **39**, 84 (1953).

² Furburg, S., *Acta Chem. Scand.*, **6**, 634 (1952).

³ Chargaff, E., for references see Zamenhof, S., Brawerman, G., and Chargaff, E., *Biochim. et Biophys. Acta*, **9**, 402 (1952).

⁴ Wyatt, G. R., *J. Gen. Physiol.*, **36**, 201 (1952).

⁵ Astbury, W. T., *Symp. Soc. Exp. Biol.*, **1**, Nucleic Acid, 66 (Camb. Univ. Press, 1947).

⁶ Wilkins, M. H. F., and Randall, J. T., *Biochim. et Biophys. Acta*, **10**, 192 (1953).

Molecular Structure of Deoxypentose Nucleic Acids

WHILE the biological properties of deoxypentose nucleic acid suggest a molecular structure containing great complexity, X-ray diffraction studies described here (cf. Astbury¹) show the basic molecular configuration has great simplicity. The purpose of this communication is to describe, in a preliminary way, some of the experimental evidence for the polynucleotide chain configuration being helical, and existing in this form when in the natural state. A fuller account of the work will be published shortly.

The structure of deoxypentose nucleic acid is the same in all species (although the nitrogen base ratios alter considerably) in nucleoprotein, extracted or in cells, and in purified nucleate. The same linear group of polynucleotide chains may pack together parallel in different ways to give crystalline¹⁻³, semi-crystalline or paracrystalline material. In all cases the X-ray diffraction photograph consists of two regions, one determined largely by the regular spacing of nucleotides along the chain, and the other by the longer spacings of the chain configuration. The sequence of different nitrogen bases along the chain is not made visible.

Oriented paracrystalline deoxypentose nucleic acid ('structure B' in the following communication by Franklin and Gosling) gives a fibre diagram as shown in Fig. 1 (cf. ref. 4). Astbury suggested that the strong 3.4-Å reflexion corresponded to the internucleotide repeat along the fibre axis. The ~34 Å layer lines, however, are not due to a repeat of a polynucleotide composition, but to the chain configuration repeat, which causes strong diffraction as the nucleotide chains have higher density than the interstitial water. The absence of reflexions on or near the meridian immediately suggests a helical structure with axis parallel to fibre length.

Diffraction by Helices

It may be shown⁵ (also Stokes, unpublished) that the intensity distribution in the diffraction pattern of a series of points equally spaced along a helix is given by the squares of Bessel functions. A uniform continuous helix gives a series of layer lines of spacing corresponding to the helix pitch, the intensity distribution along the n th layer line being proportional to the square of J_n , the n th order Bessel function. A straight line may be drawn approximately through

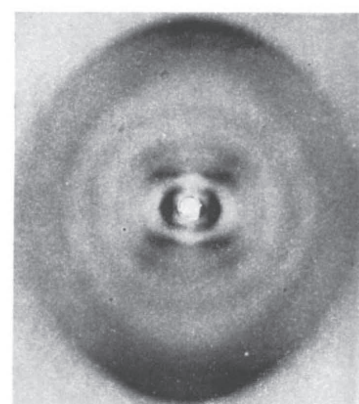


Fig. 1. Fibre diagram of deoxypentose nucleic acid from *B. coli*. Fibre axis vertical

the innermost maxima of each Bessel function and the origin. The angle this line makes with the equator is roughly equal to the angle between an element of the helix and the helix axis. If a unit repeats n times along the helix there will be a meridional reflexion (J_0^2) on the n th layer line. The helical configuration produces side-bands on this fundamental frequency, the effect⁶ being to reproduce the intensity distribution about the origin around the new origin, on the n th layer line, corresponding to C in Fig. 2.

We will now briefly analyse in physical terms some of the effects of the shape and size of the repeat unit or nucleotide on the diffraction pattern. First, if the nucleotide consists of a unit having circular symmetry about an axis parallel to the helix axis, the whole diffraction pattern is modified by the form factor of the nucleotide. Second, if the nucleotide consists of a series of points on a radius at right-angles to the helix axis, the phases of radiation scattered by the helices of different diameter passing through each point are the same. Summation of the corresponding Bessel functions gives reinforcement for the inner-

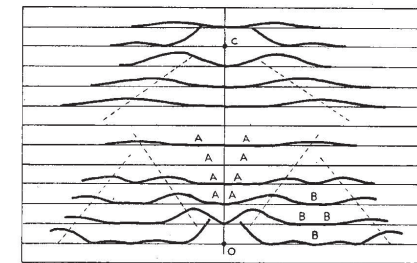
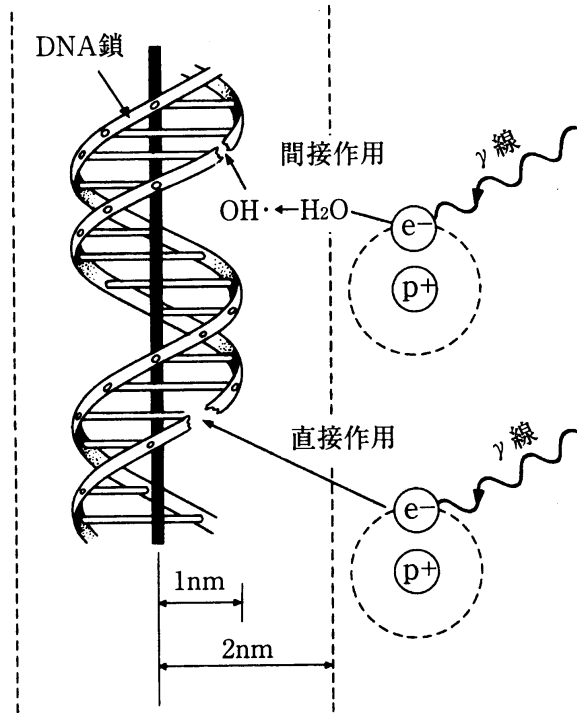
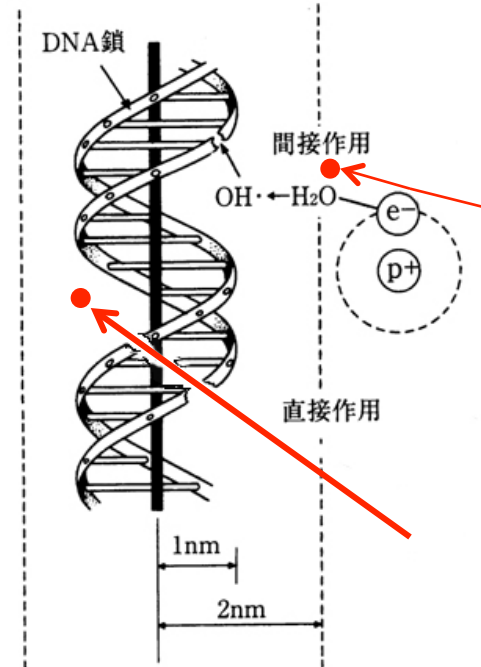


Fig. 2. Diffraction pattern of system of helices corresponding to structure of deoxypentose nucleic acid. The squares of Bessel functions are plotted about 0 on the equator and on the first, second, third and fifth layer lines for half of the nucleotide mass at 20 Å diameter and remainder distributed along a radius, the mass at a given radius being proportional to the radius. About C on the tenth layer line similar functions are plotted for an outer diameter of 12 Å.

電離放射線や紫外線はDNAを傷つける。



直接作用と間接作用の概念図

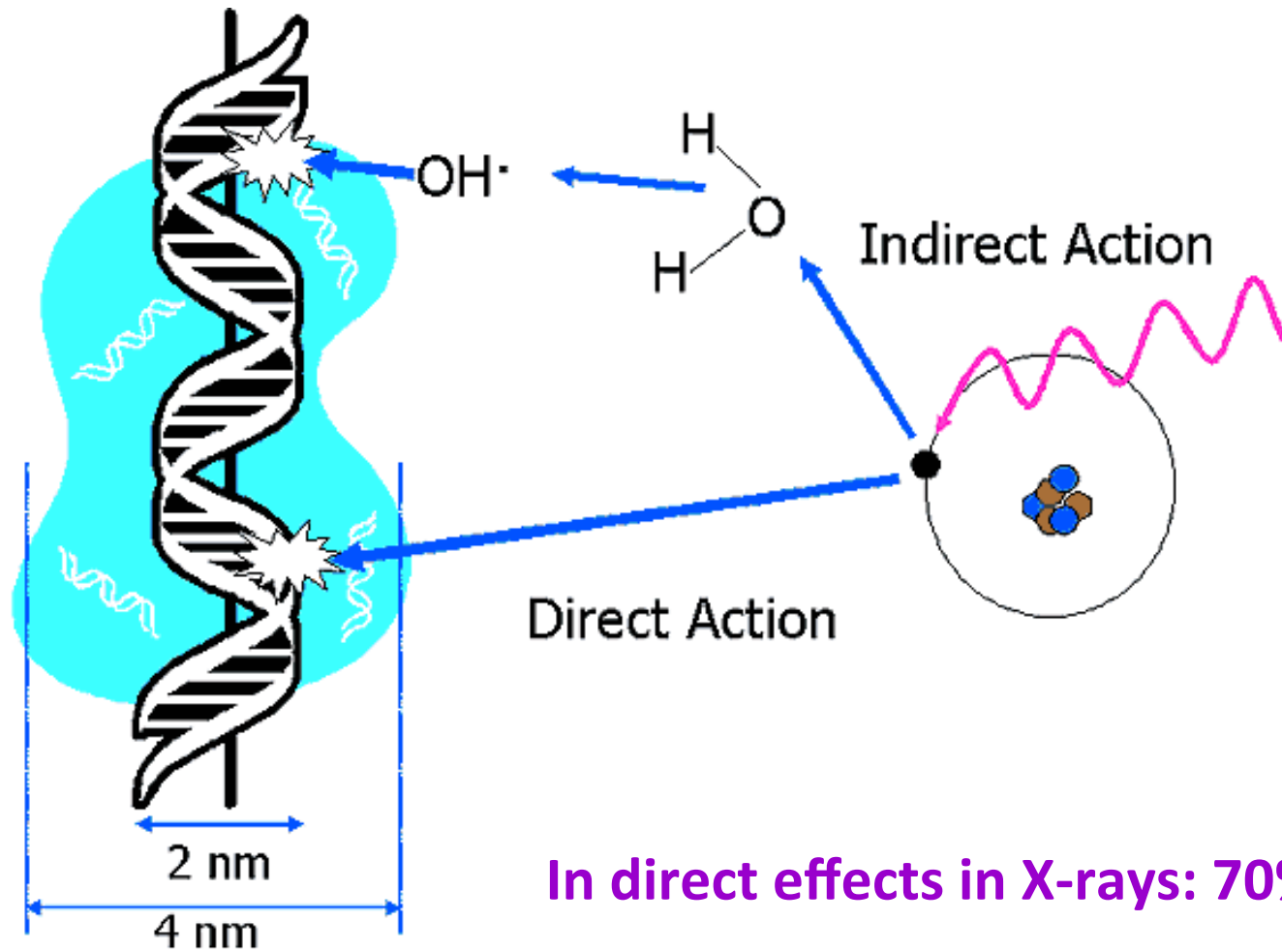


直接作用と間接作用の概念図

(E. Hall より)

標的はDNA

Direct and indirect actions of ionizing radiation

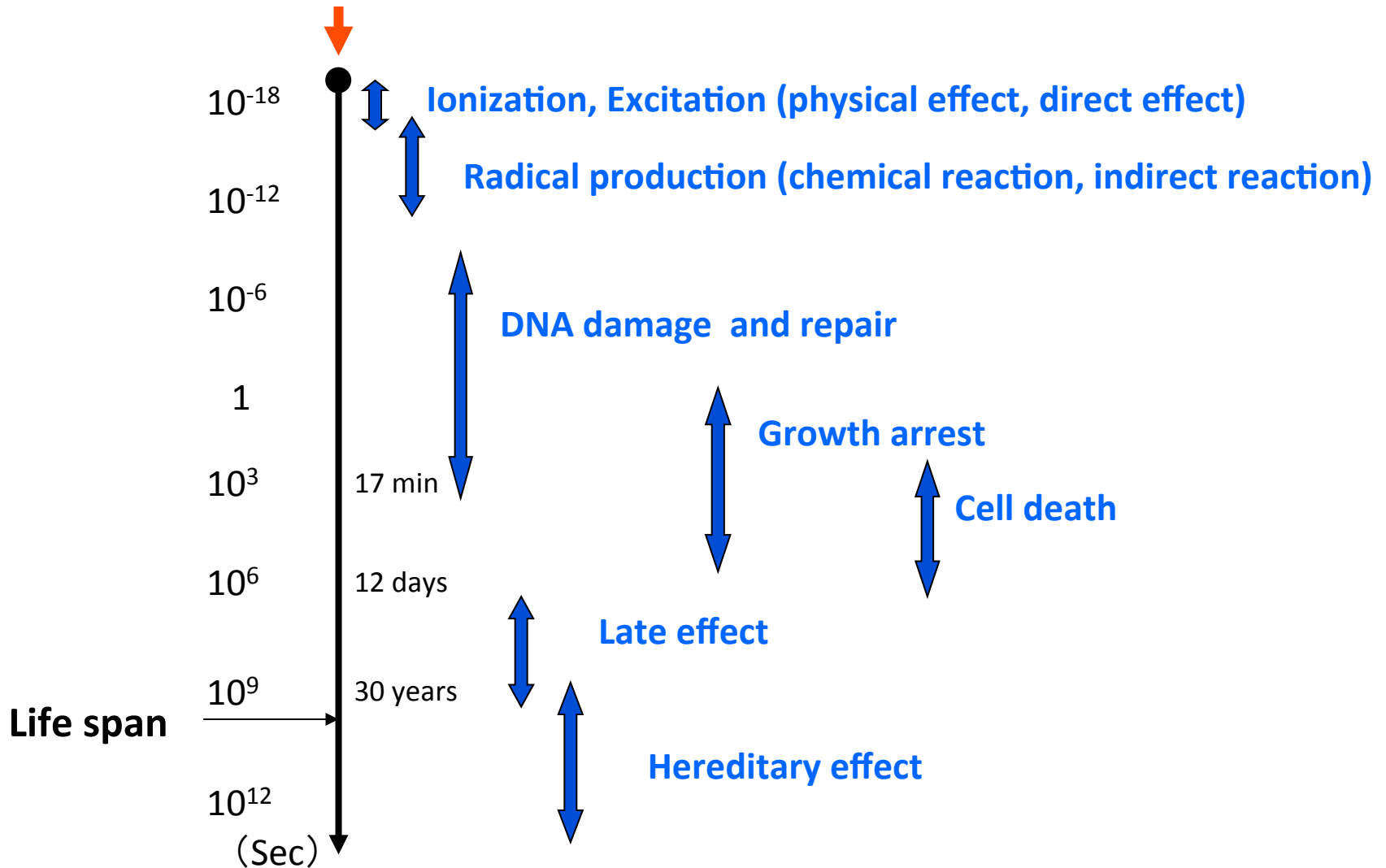


In direct effects in X-rays: 70%

Proton beams



Ionizing Radiation

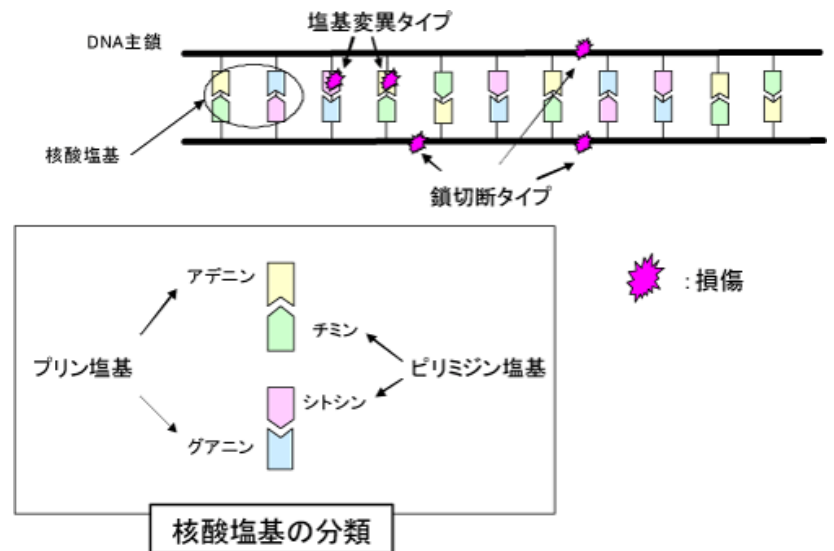
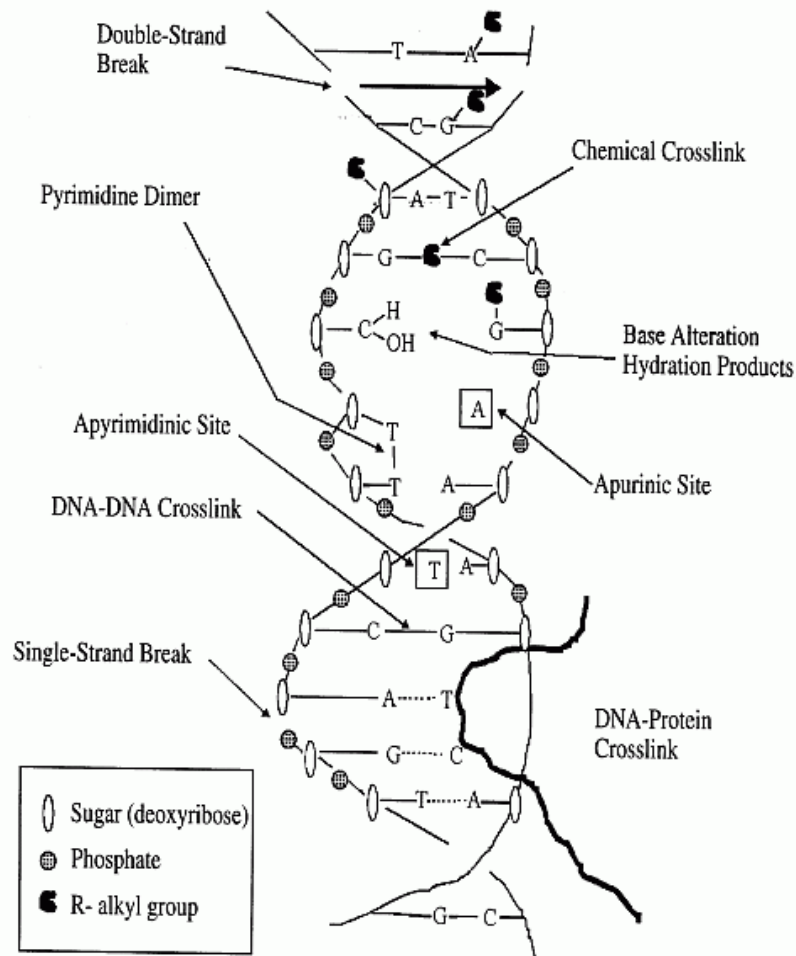


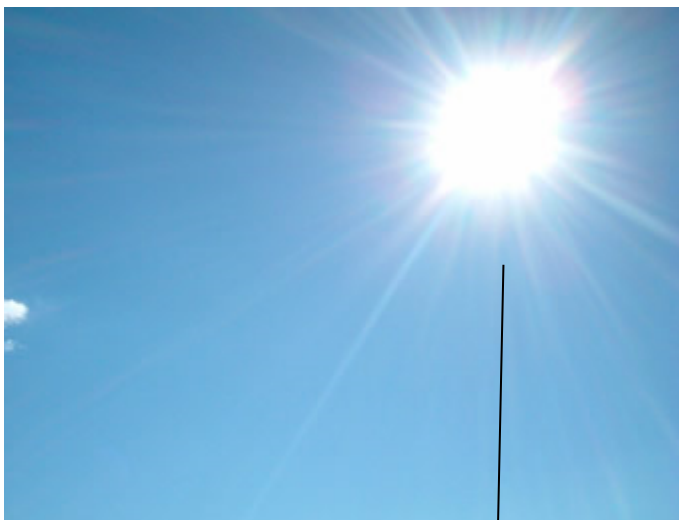
DNA損傷

塩基の傷

糖鎖の傷

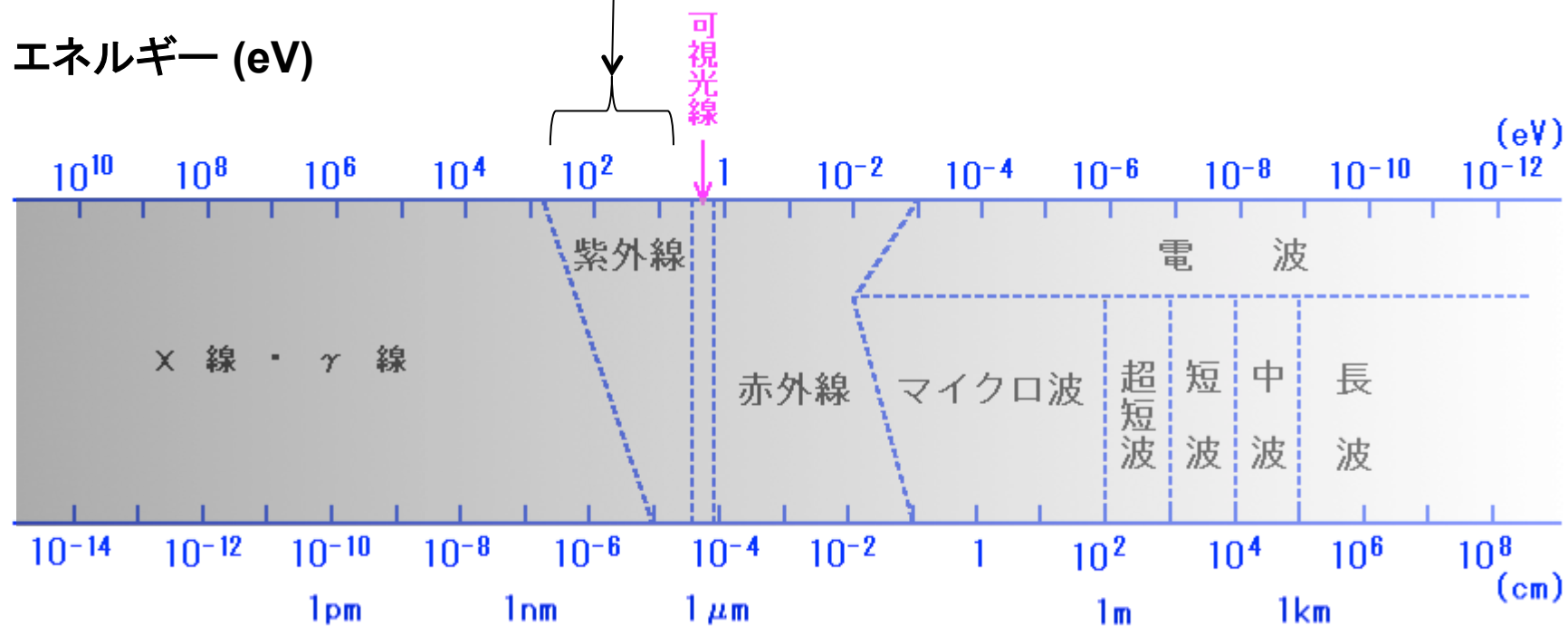
DNA損傷の種類





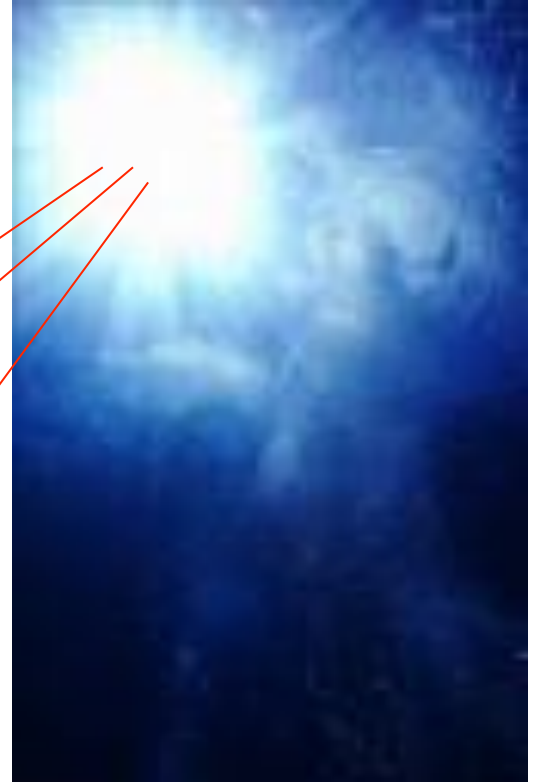
紫外線

エネルギー (eV)

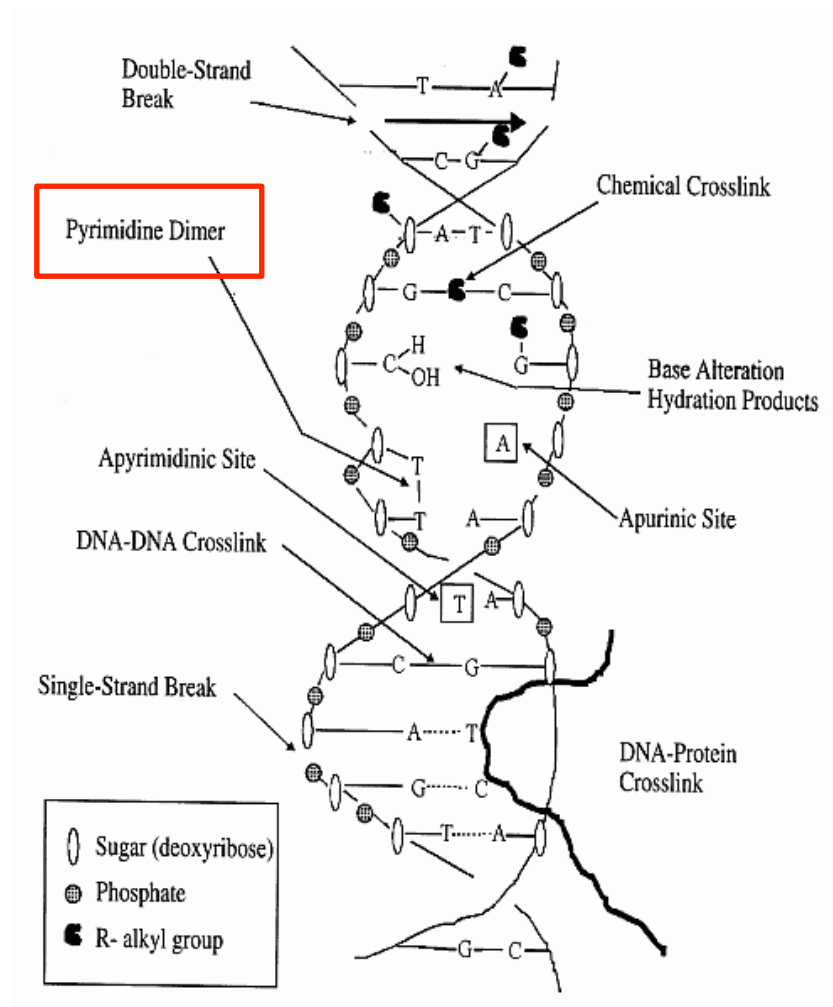


波長 (cm)

紫外線はDNAを傷つける。



紫外線はDNAにピリミジン二量体を作る。



真夏の日光浴で背中中の細胞1個、1時間あたりに生じるピリミジン二量体はどれくらいでしょうか？

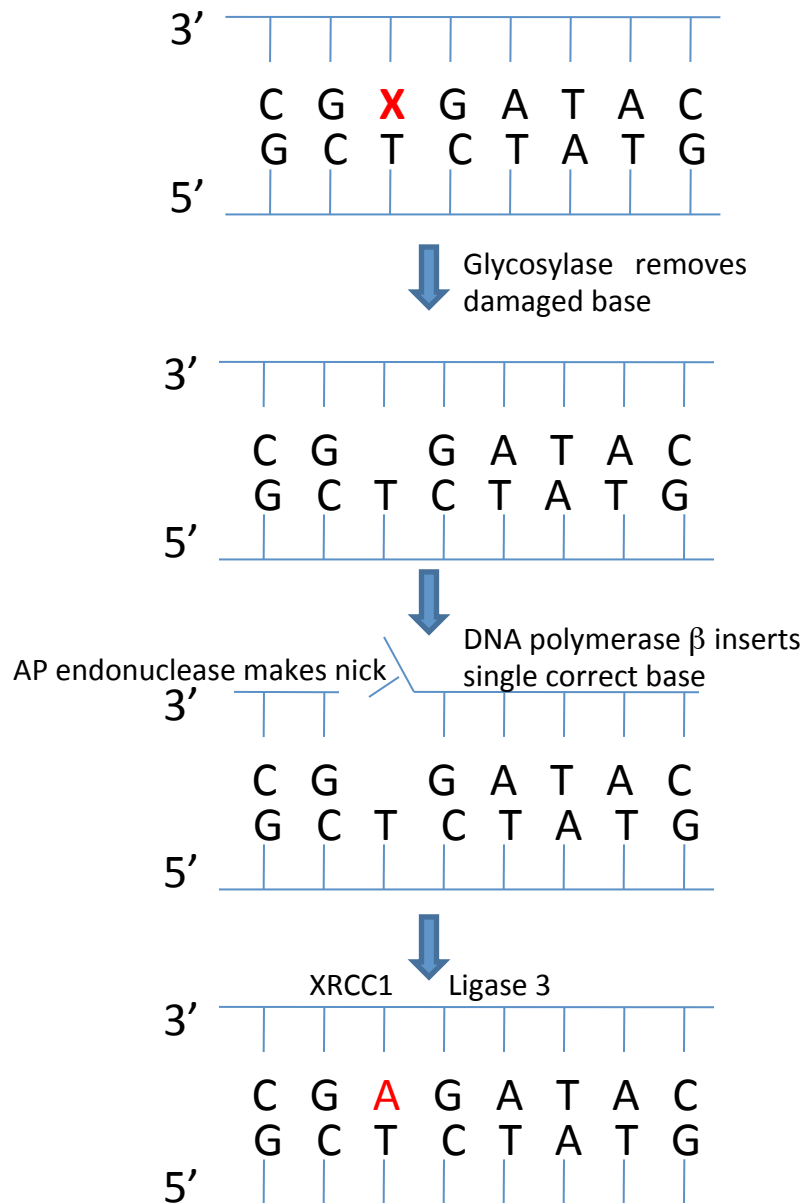
1. 10
2. 100
3. 1,000
4. 10,000

人体細胞のDNAに自然発生する傷の種類と数

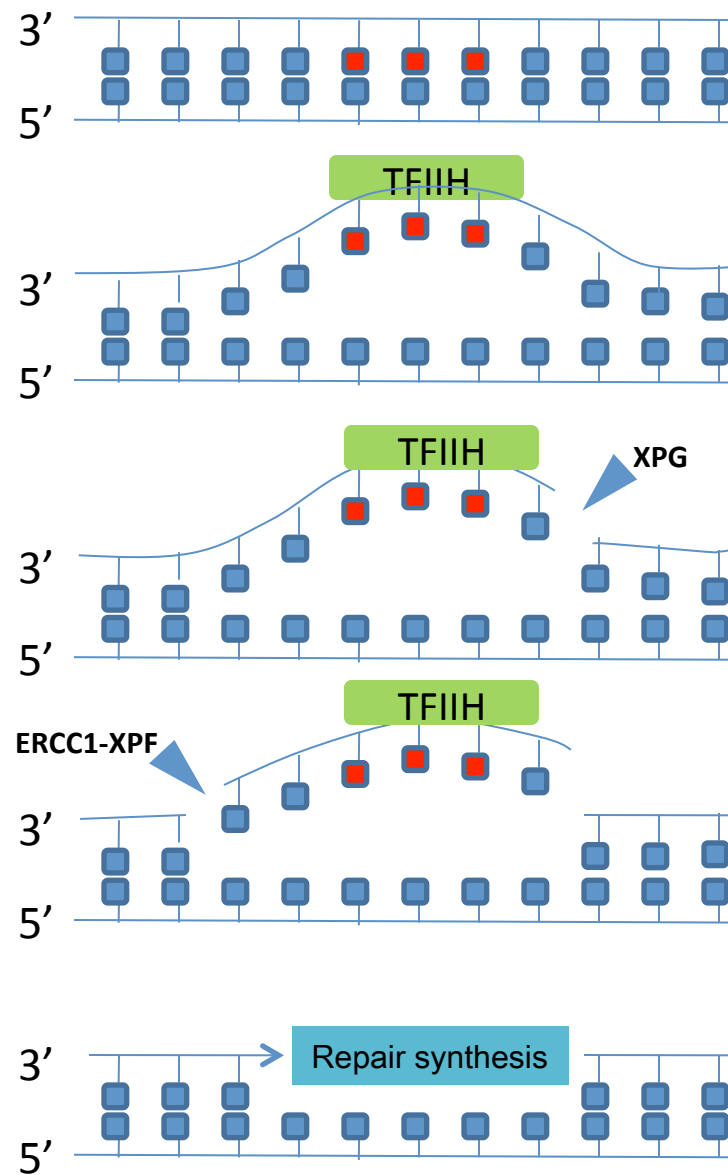
自然要因	傷の種類	件数/細胞/時間
酸素	グアニン8位の酸化	25
	チミングリコール	20
	シトシンの脱アミノ	10
紫外線 (真夏の昼)	ピリミジン二量体	10,000
各種要因	1本鎖切断	2,000
	プリン塩基の喪失	600
	ピリミジン塩基の喪失	30
	グアニン6位酸素のメチル化	100

DNA damage and repair

塩基除去修復

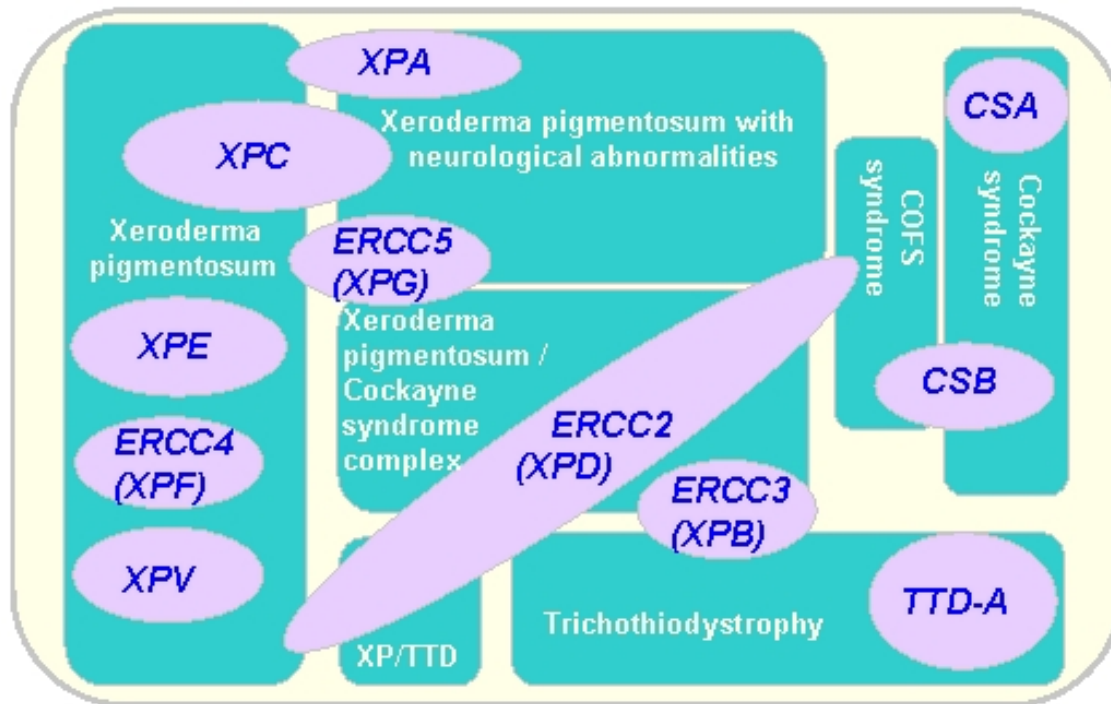


ヌクレチド除去修復



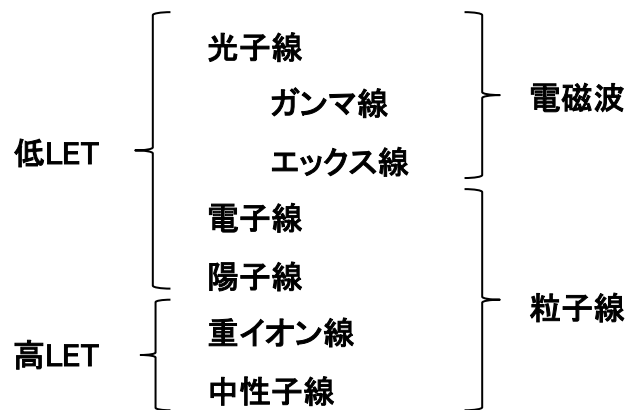
色素性乾皮症

主にXPA遺伝子の異常

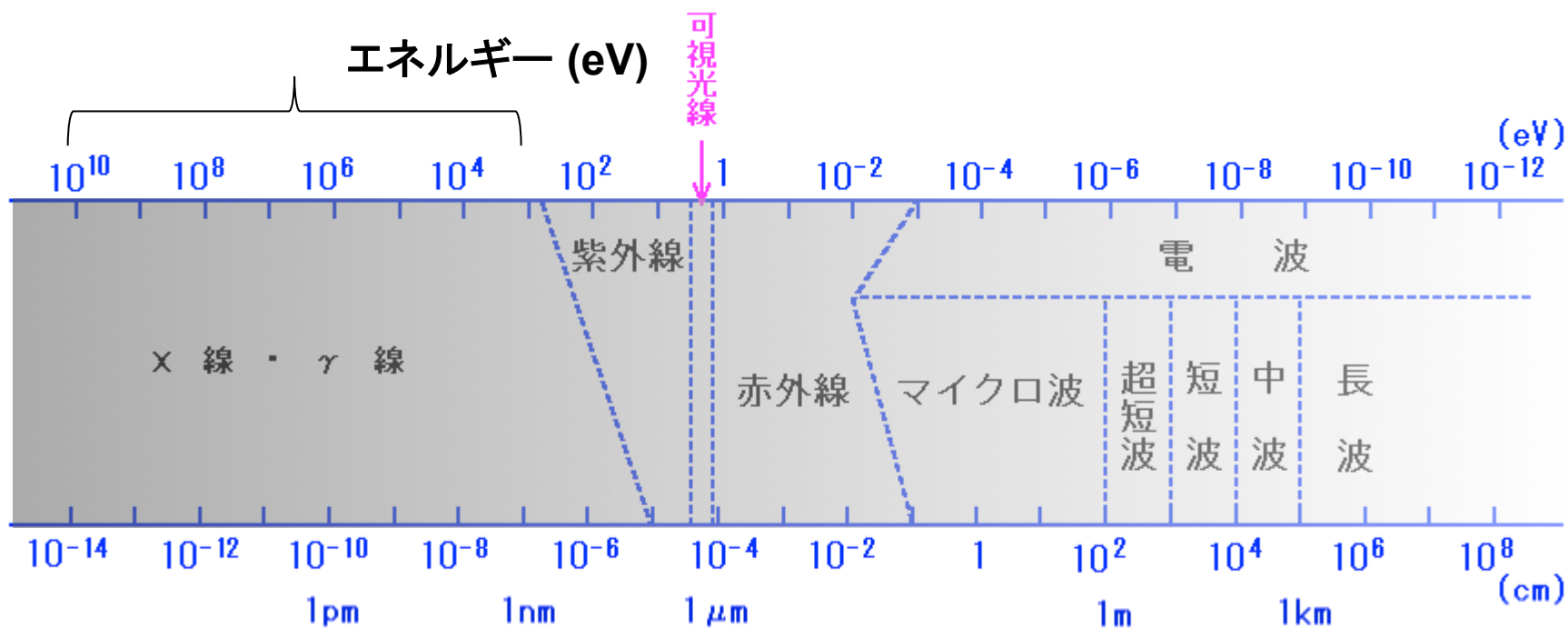


Kenneth H Kraemer, MDBasic Research Laboratory
Center for Cancer Research, National Cancer Institute
Bethesda kraemer@nih.gov

Initial Posting: June 20, 2003; Last Update: April 22, 2008.

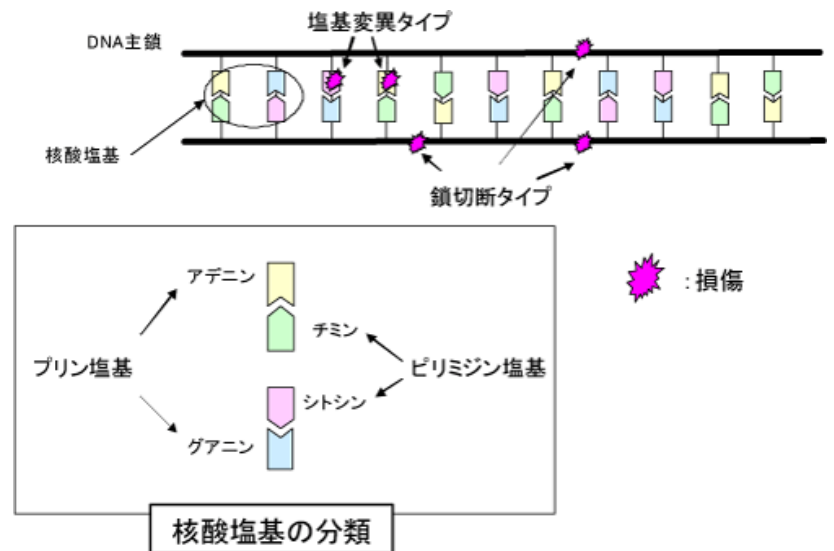
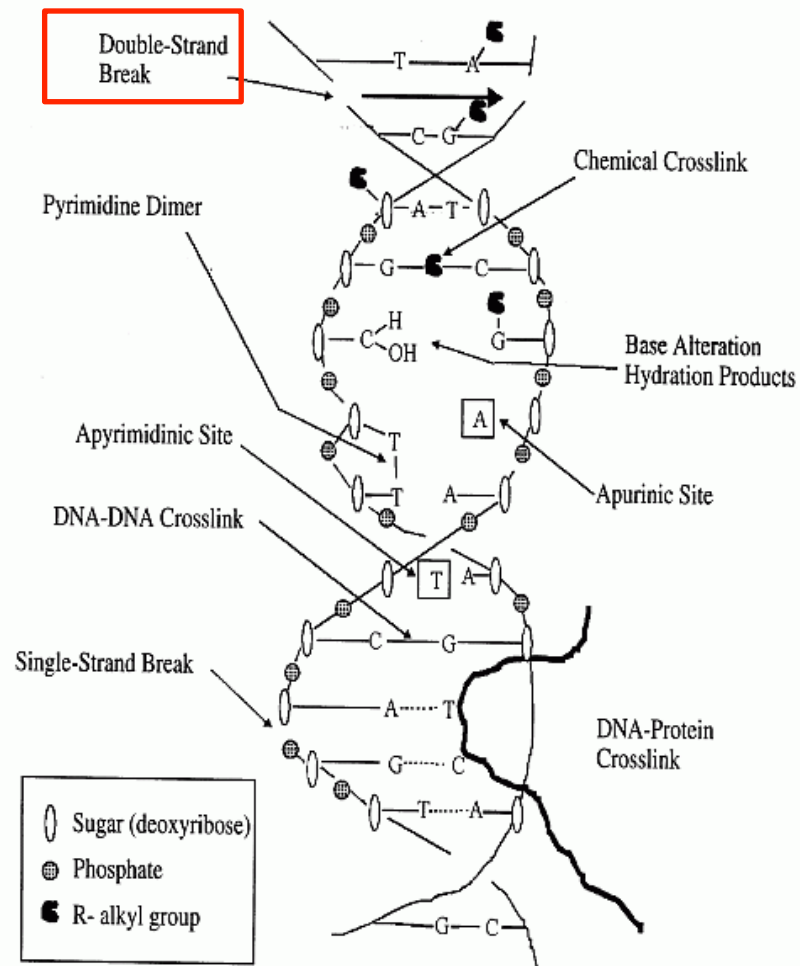


電離放射線



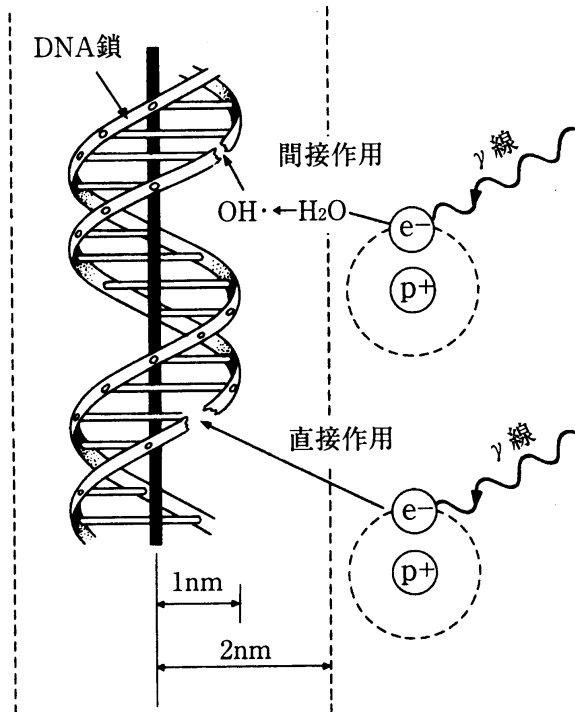
波長 (cm)

DNA損傷の種類

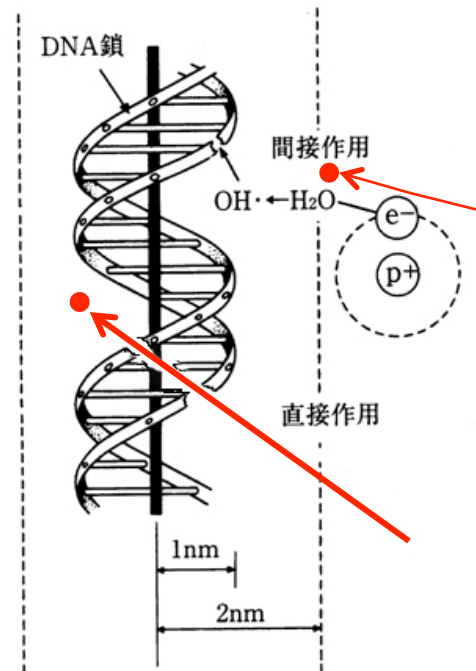


DNA二本鎖切断

DNA糖鎖切断

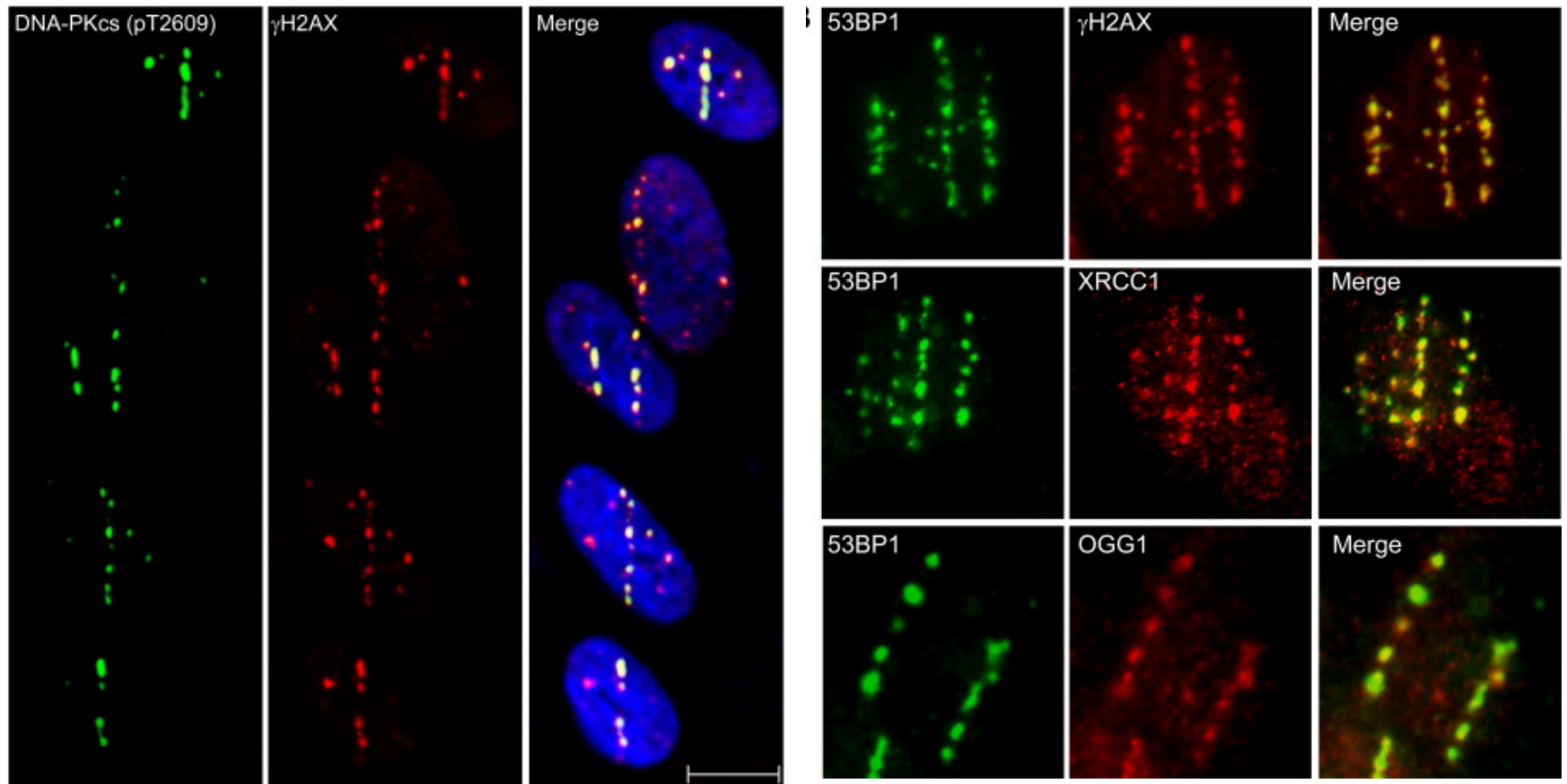


直接作用と間接作用の概念図



直接作用と間接作用の概念図

(E. Hall より)

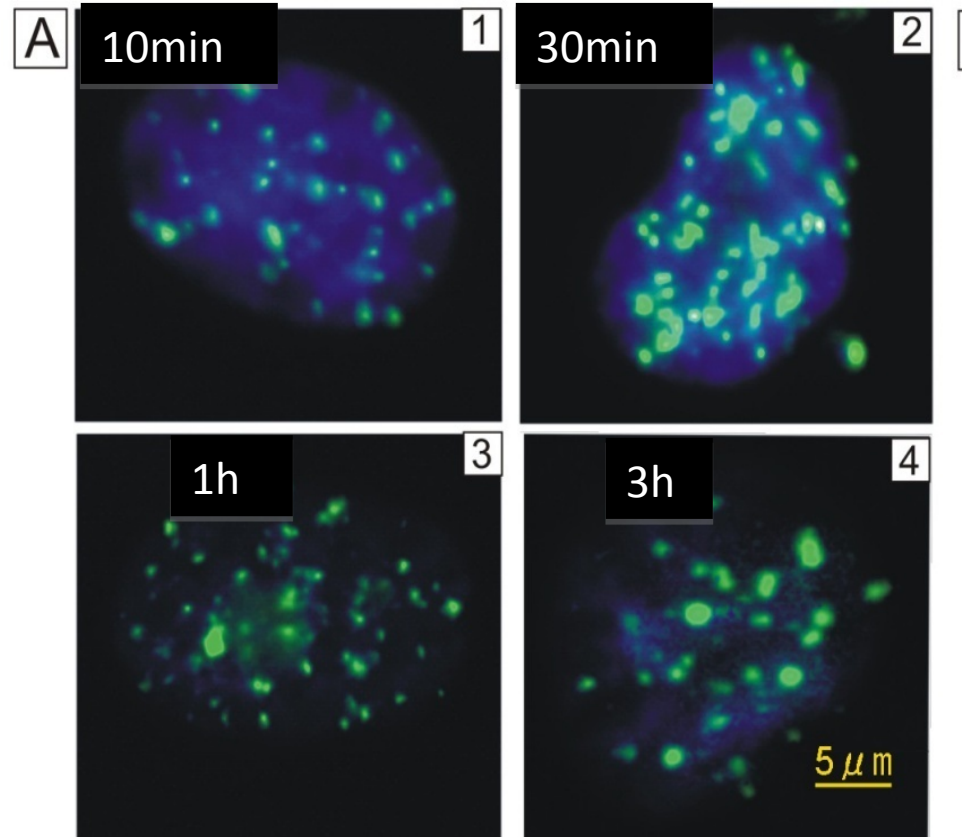
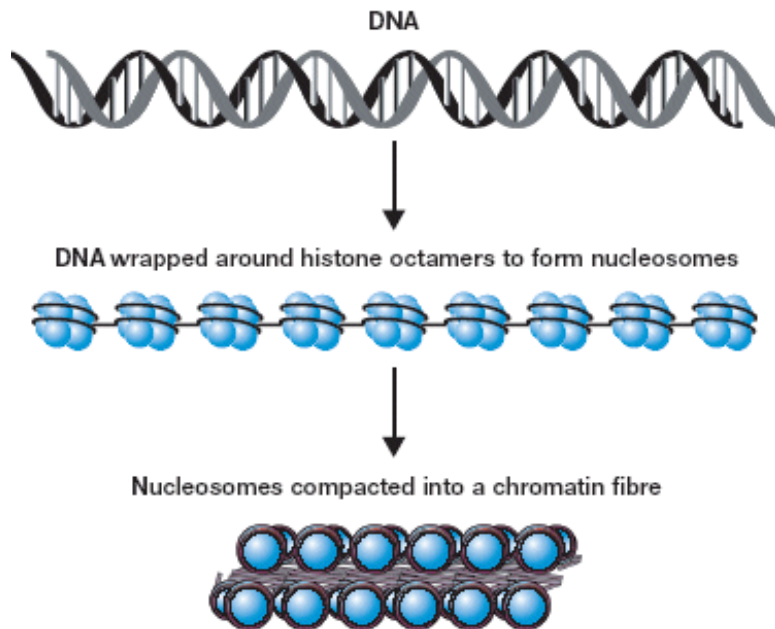


Asaithmby and Chen DJ, Mechanism of cluster DNA damage repair in response to high-atomic number and energy particles radiation. Mutation Res 2010

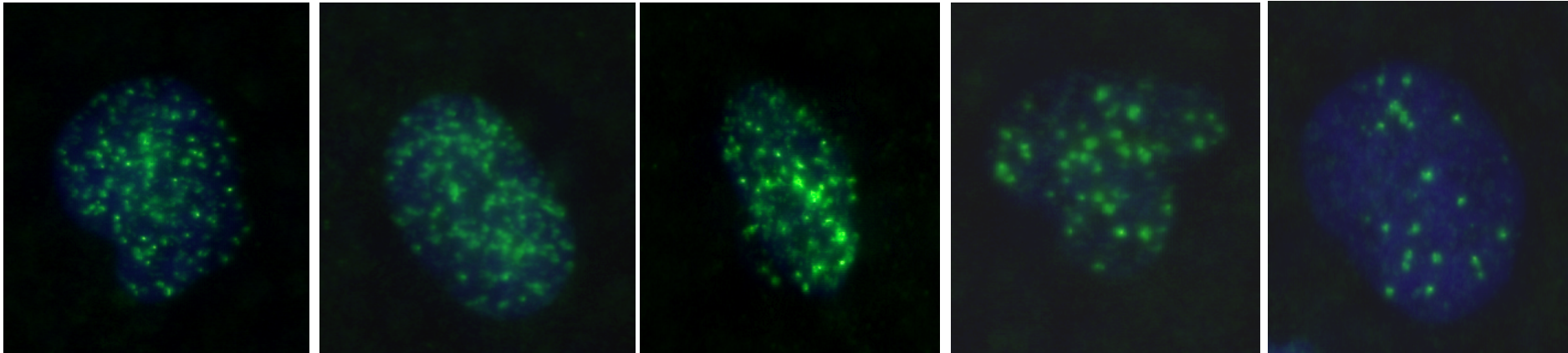
DNA二本鎖切斷

γ -H2AX foci formation

ONS76 / Proton beam 2Gy



γ -H2AX foci formation in ONS76 after 2 Gy of proton irradiation



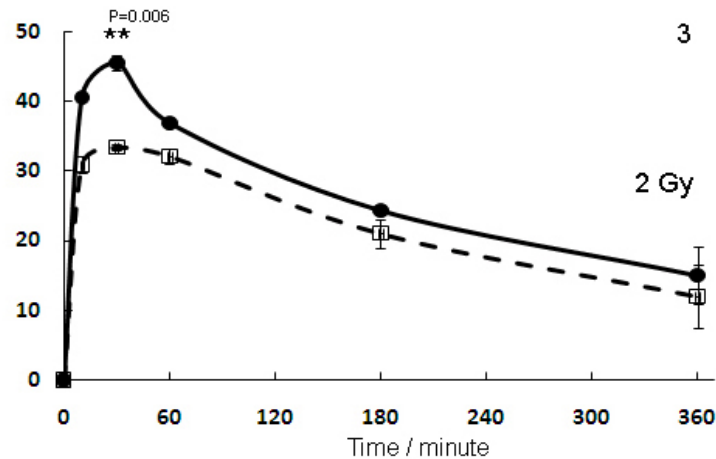
10 min

30 min

60 min

180 min

240 min



DNA二本鎖切断修復

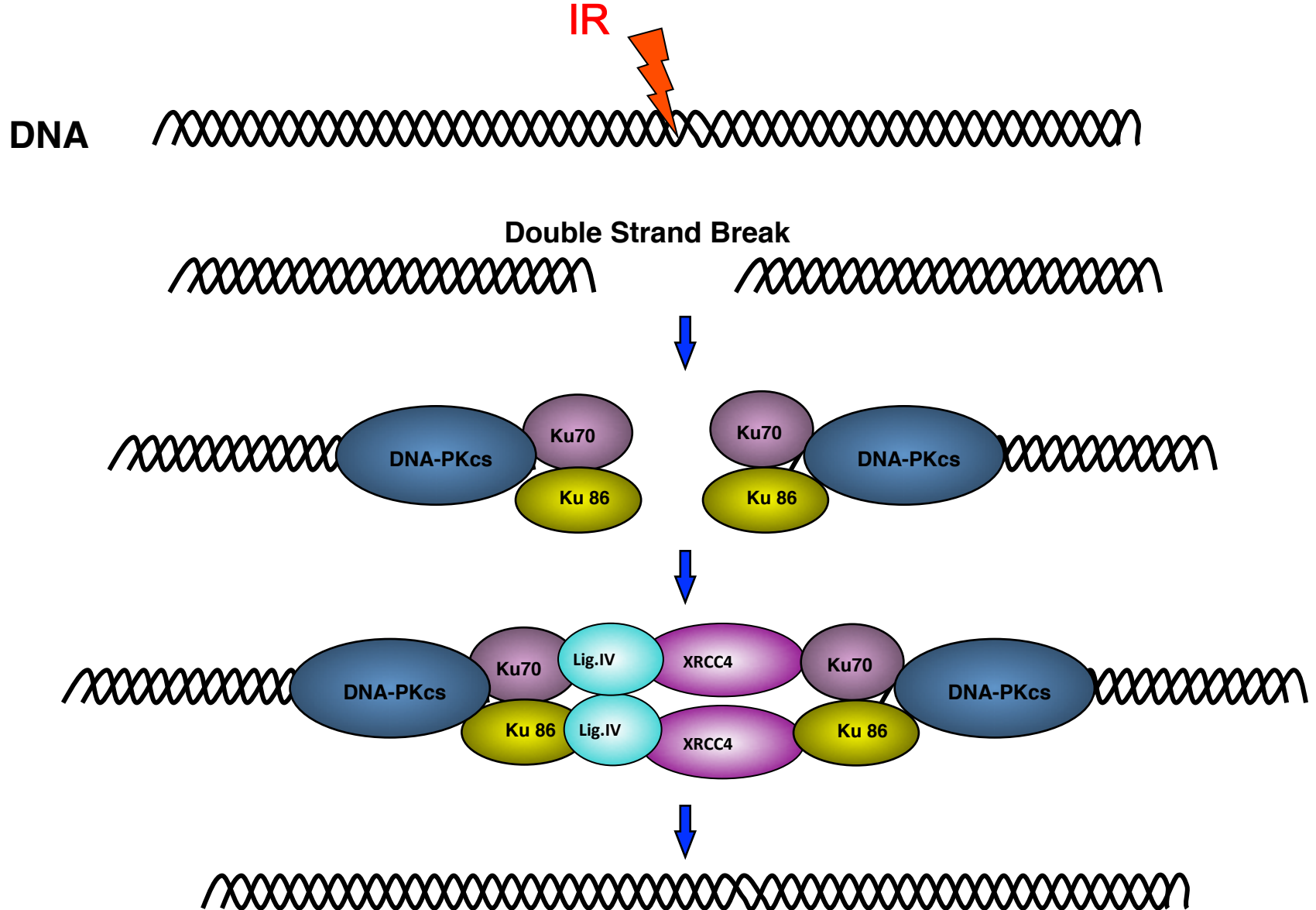
非相同末端再結合

Non-homologous end joining (NHEJ)

相同組換え

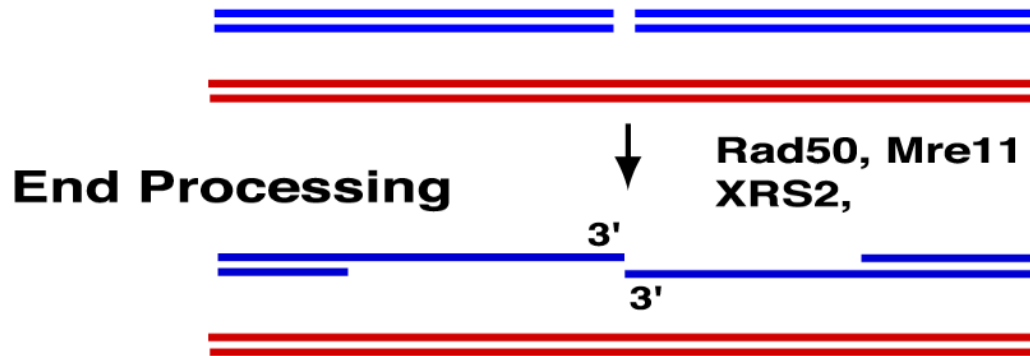
Homologous recombination repair (HRR)

非相同末端再結合 Non-homologous end joining (NHEJ)



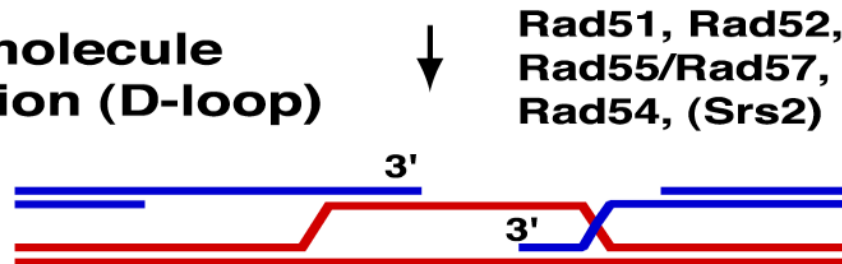
相同組換え Homologous recombination

DSB Formation



RPA
NBS1
RAD51

Joint molecule formation (D-loop)



Strand invasion and
exchange between donor
and recipient

Repair DNA synthesis (Srs2)
Resolution of Intermediates (Srs2)
Ligation

Mature Recombinants

DNA二本鎖切断修復

非相同末端再結合

Non-homologous end joining (NHEJ)

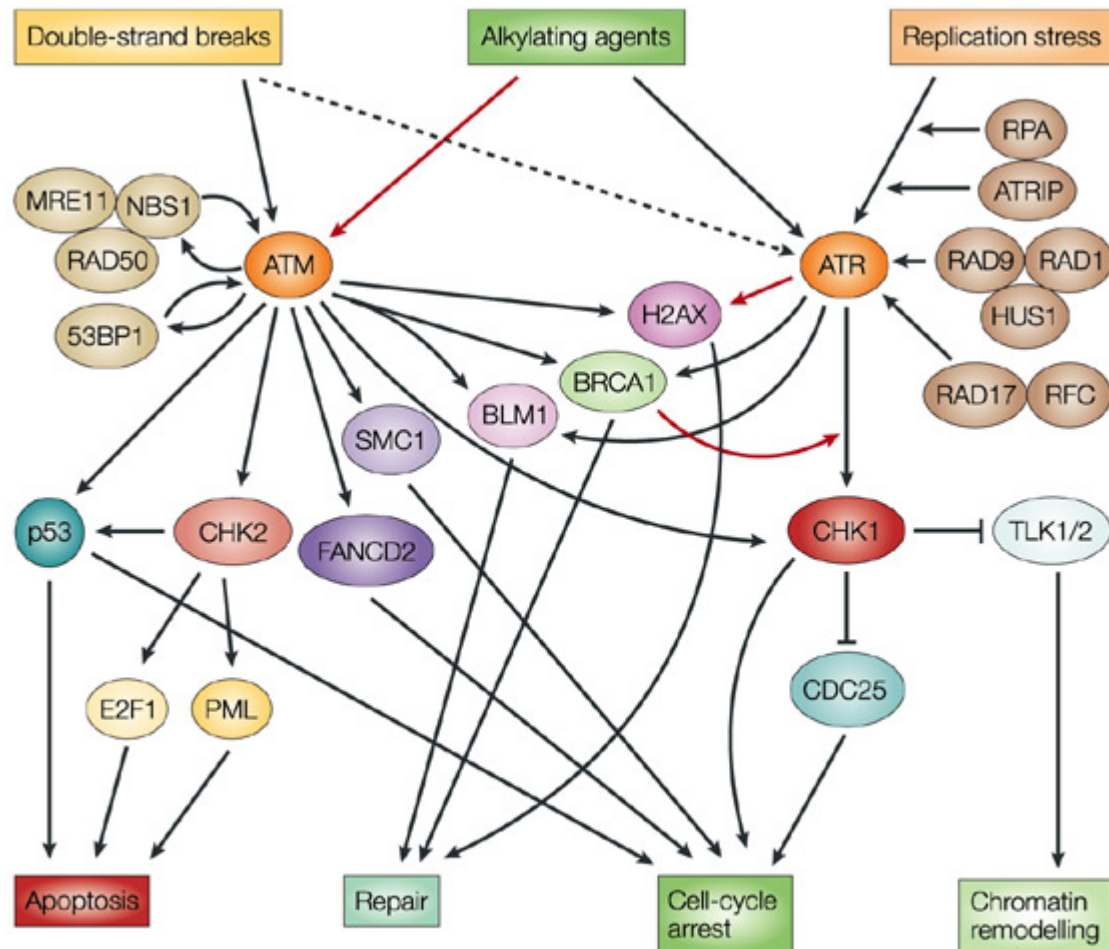
- 1 切断端同士の再結合
- 2 細胞周期にかかわらず常に起きる。
- 3 再結合の際の精度がHRRより低く、mismatchが起きる可能性がある。
- 4 ほとんどのDNA2本鎖切断の修復はNHEJにより行われる。

相同組換え

Homologous recombination repair (HRR)

- 1 断端のない相同配列を鋳型にしたDNA組み換え
- 2 S、G2 期に起きる。
- 3 修復の精度が高い。
- 4 頻度は低い。

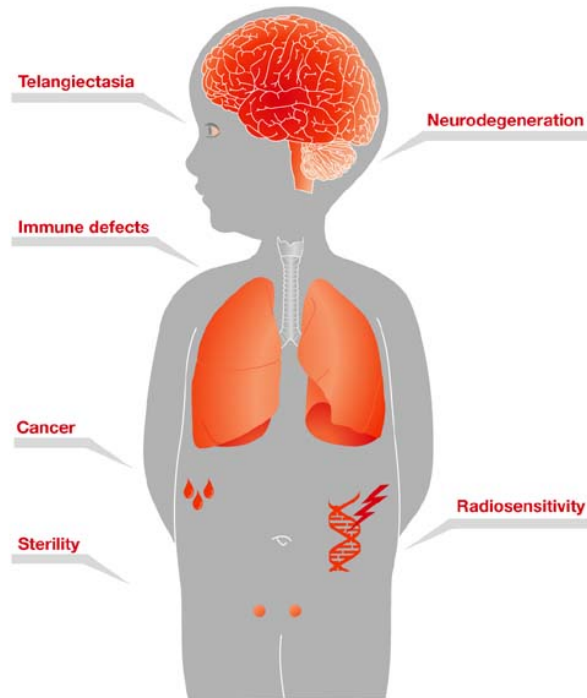
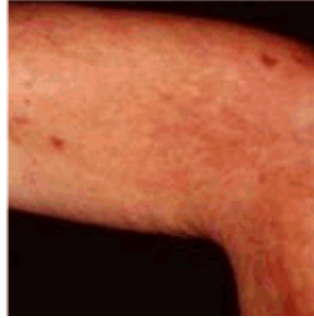
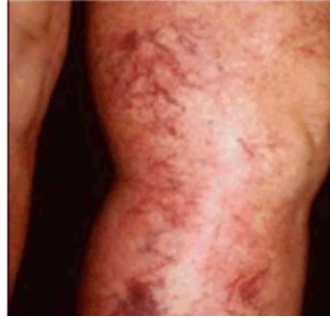
DNA damage response signal-transduction network



Nature Reviews | Cancer

Nature Review Cancer 2004

Ataxia Telangiectasia



・概要

歩行開始時から明らかになる進行性運動失調症、免疫不全症、高頻度の腫瘍発生、内分泌異常症、放射線高感受性、毛細血管拡張などを特徴とする、多臓器に渡る障害が進行性に認められる遺伝疾患である。

2. 疫学

患者数100人～1000人、人口10-15万人に1人、保因者は人口の0.5-1%。

3. 原因

1995年にATM(Ataxia telangiectasia mutated)遺伝子が、Ataxia telangiectasiaの責任遺伝子として同定された。遺伝子は11q22.3に位置し、66のエクソンからなり、全長150KBのゲノムDNAから成る。遺伝子産物であるATMはDNA損傷修復応答の鍵となる分子である。

4. 症状

歩行開始と共に明らかになる歩行失調(体幹失調)、小脳性構語障害・流涎、眼球運動の失行、眼振、眼球結膜・皮膚の毛細血管拡張(6歳までに50%で明らかに。8歳時までにほぼ全例)、易感染性・免疫不全症状、高頻度の悪性腫瘍発生を認める。その他、発育不良や内分泌異常を認めることがある。

ナイミーヘン症候群



ナイミーヘン症候群はナイミーヘン大学小児科(オランダ)で1981年に最初に報告された。これは単一の劣性遺伝子の疾患である。患者は**東欧・中欧**を中心に約90人が報告されている。

患者は**低身長、精神発達遅滞、発育遅滞、小頭症、先天性奇形、鳥様顔貌、卵巣発育不全、免疫不全**などの症状を示す。ただし、小頭症は全患者に発生するが、その他の疾患の頻度は患者によって異なる。例えば、奇形は50%の患者に発生する。リンパ腫瘍・白血病は35%の頻度で患者に21歳以前に発生する。

患者は、若年で死亡する。X- γ 線を照射した場合の培養細胞の平均致死線量は、正常人の細胞では、1.5Gyであるのに対して、患者の細胞では0.5-0.8Gyであり、2-3倍の致死高感受性を示す。患者の末梢血リンパ球には転座や逆位が高頻度で見つかる。放射線を照射した場合の染色体異常頻度は、正常細胞に比べ患者の細胞は2.5-4倍である。正常細胞は放射線被曝後一時DNA合成が停止するが、患者の細胞はこの一時停止をしない。

DNA 修復のメカニズムと遺伝性疾患

1. DNA二本鎖切断修復:

非相同末端再結合 Non-homologous end joining (NHEJ)

DNA-PK DNA-PKcs, Ku86, Ku70

Ligase IV, xrrc4 **ATM : 小脳失調性血管拡張症**

相同組換え Homologous recombination:

rec1, RAD51, RAD52, **NBS-1: ナイミーヘン症候群**

2. 塩基除去修復:

AP endonuclease

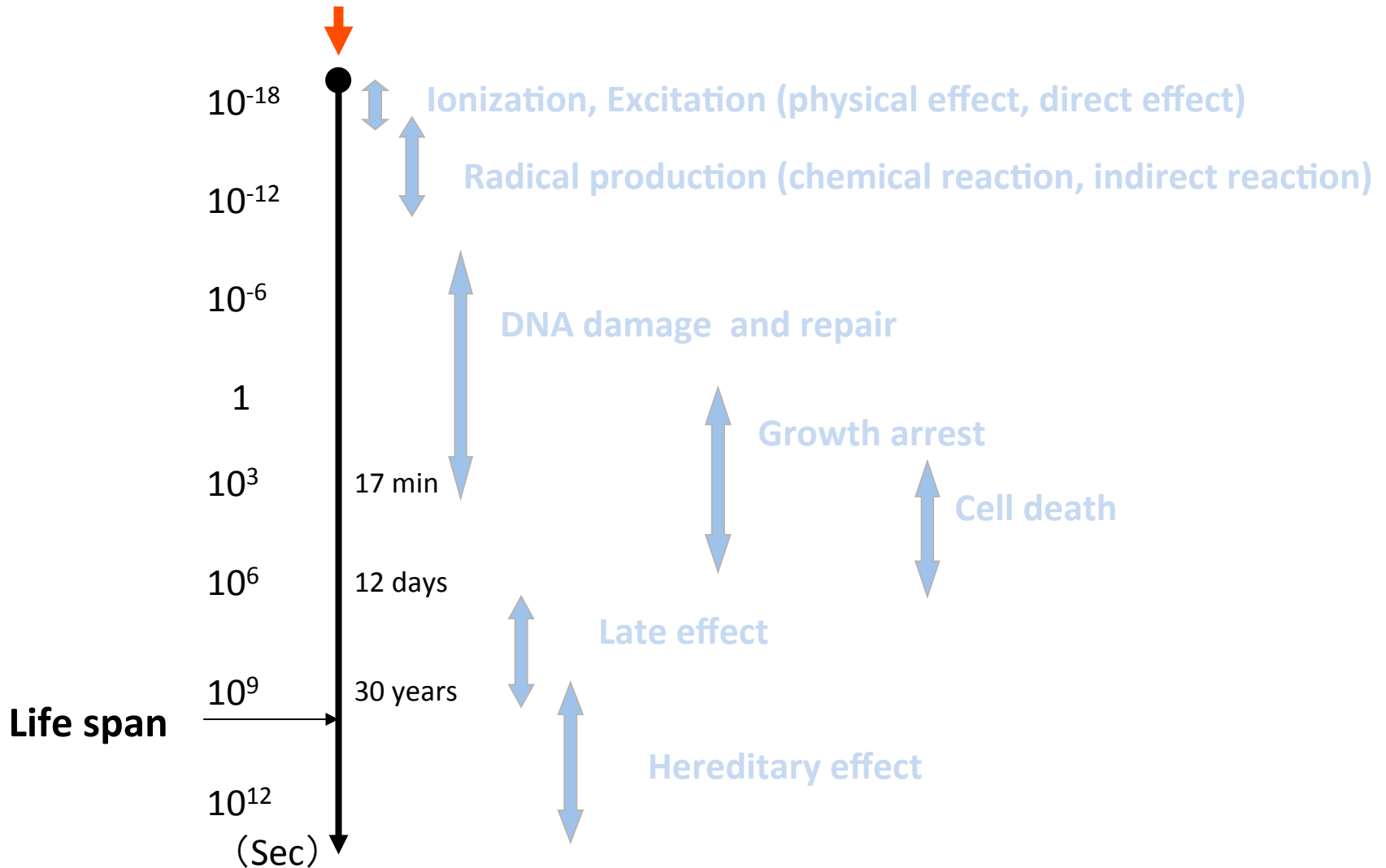
3. ヌクレオチド除去修復:

ERCC 1〜8 (XP, CS) **XPA: 色素性乾皮症**

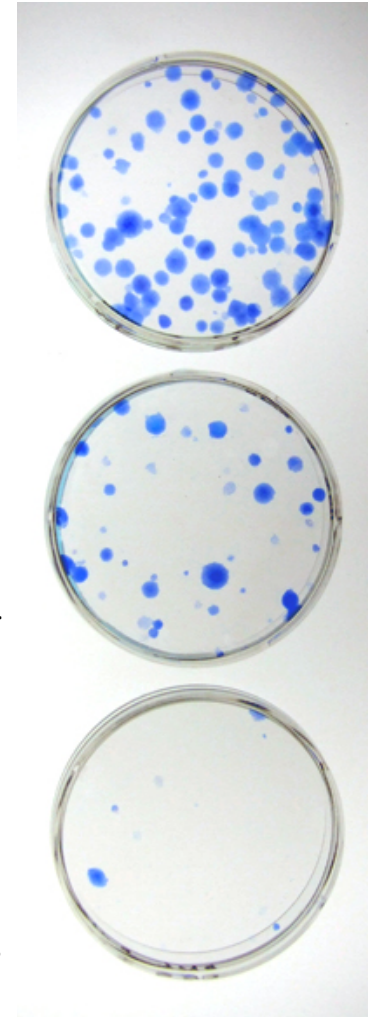
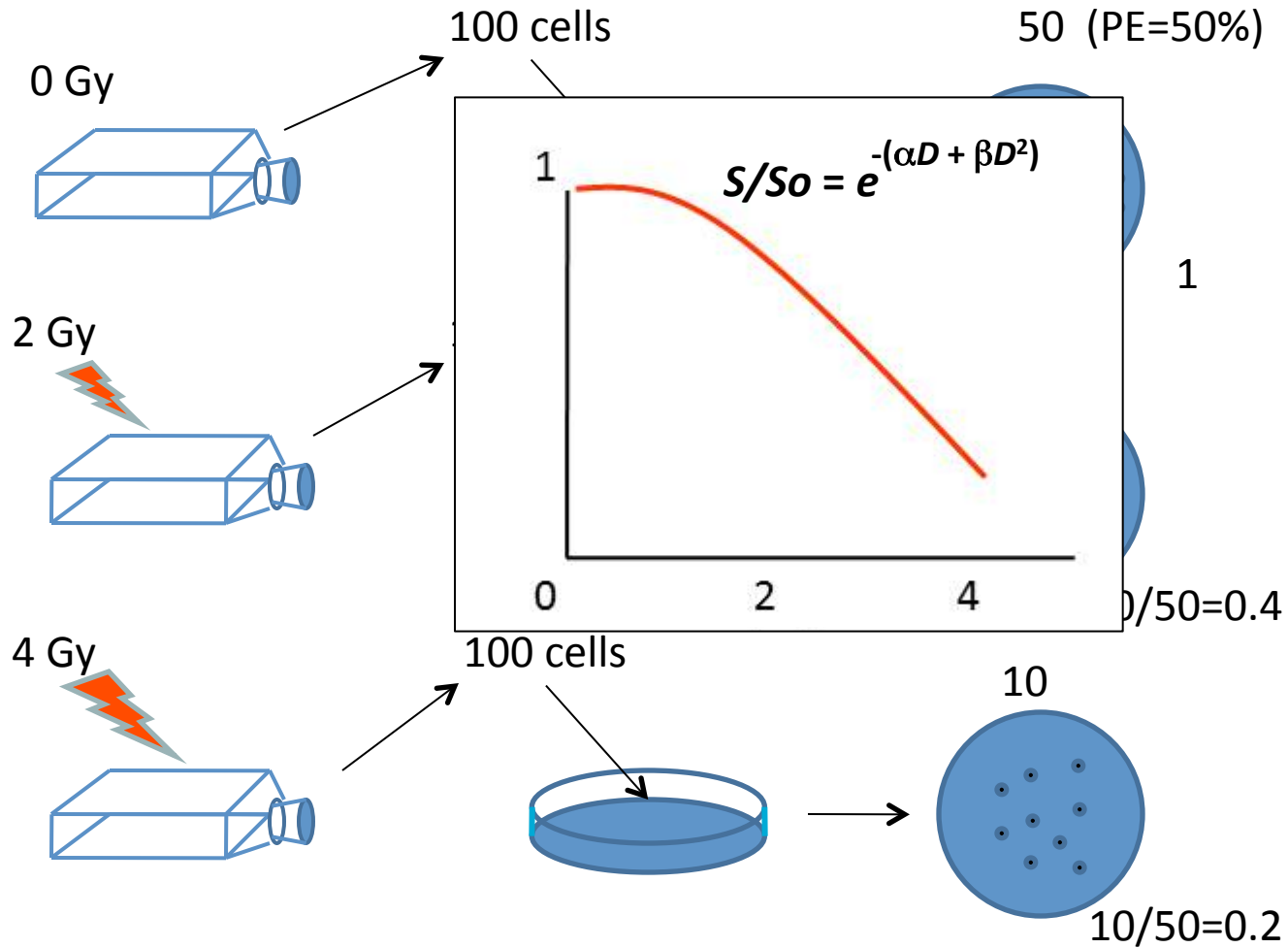
4. ミスマッチ修復:

hMSH group **遺伝性非ポリポーシス大腸がん**

Ionizing Radiation



Loss of clonogenicity after irradiation



Sensors (?)



Transducer and focus formation

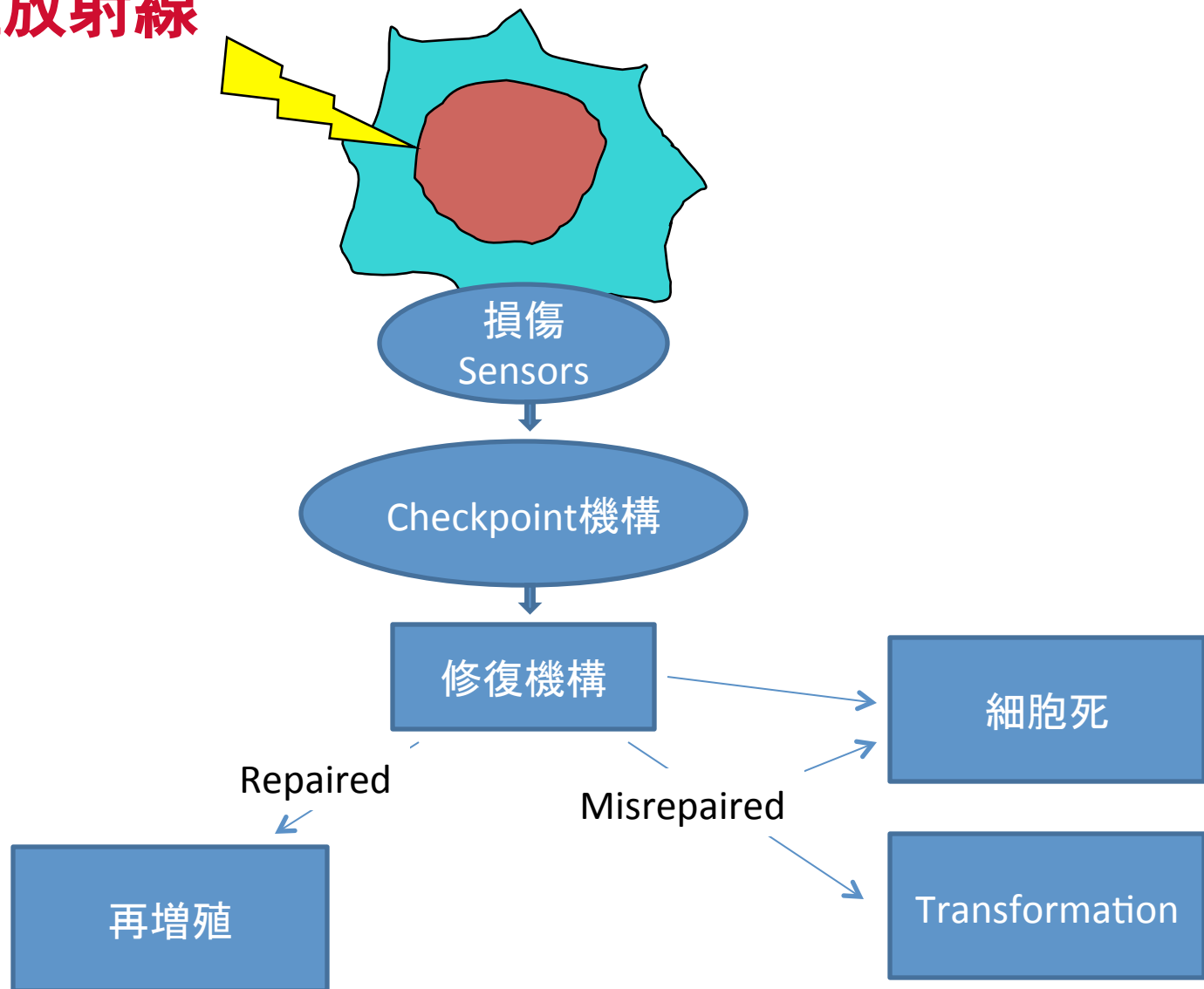
ATM (ataxia telangiectasia mutated),
ATR (ATM and Rad-3 related)
DNA-PK
MAP kinase and early responsive genes



Effectors

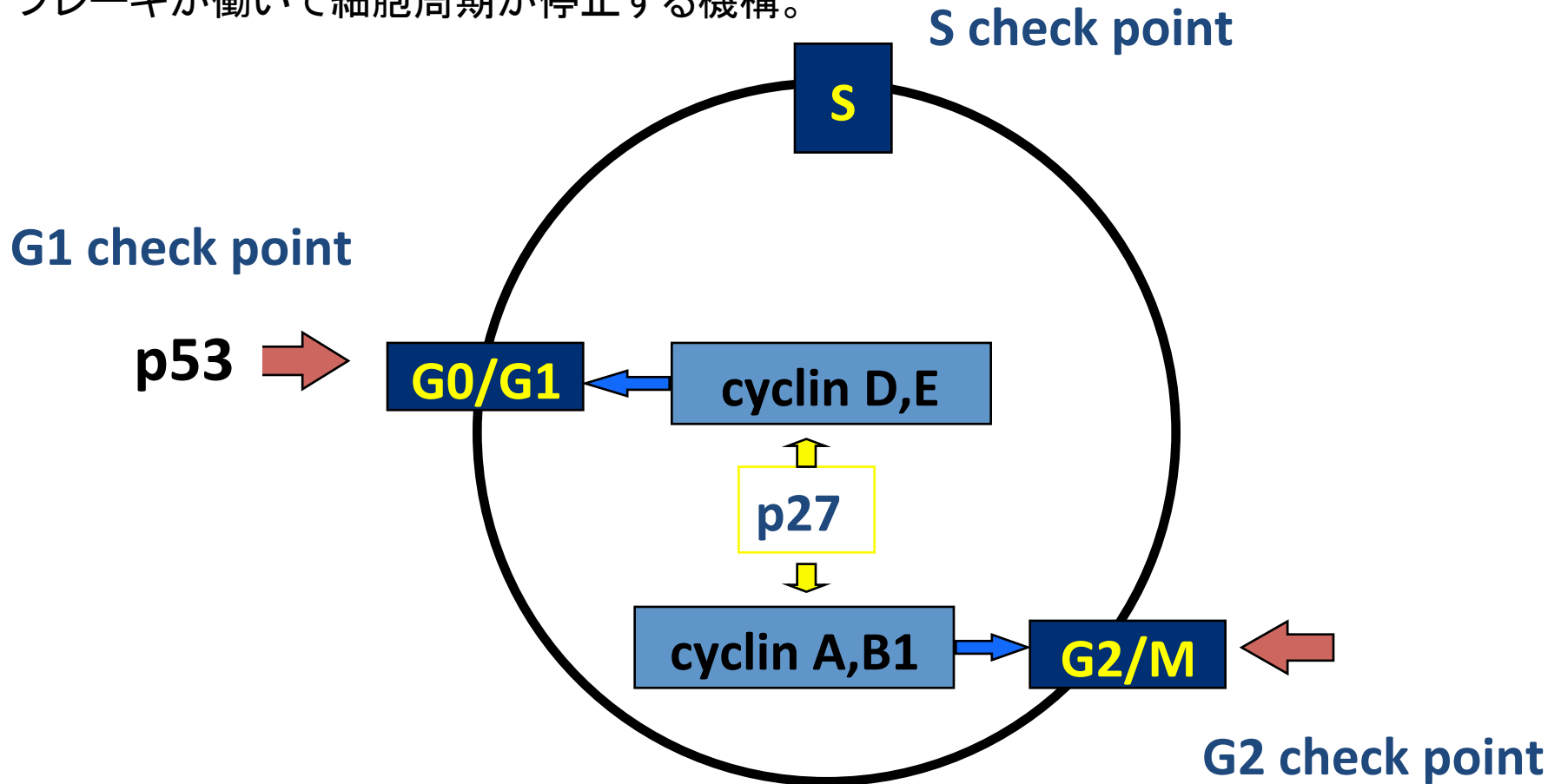
- 1. Check point**
- 2. Repair**
- 3. Cell death**

電離放射線



Check-point

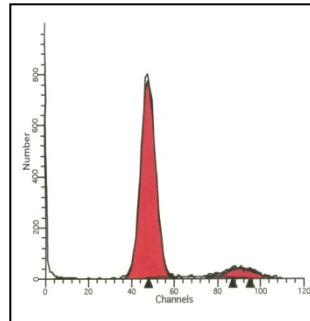
DNA損傷が感知されると、修復を行うためにブレーキが働いて細胞周期が停止する機構。



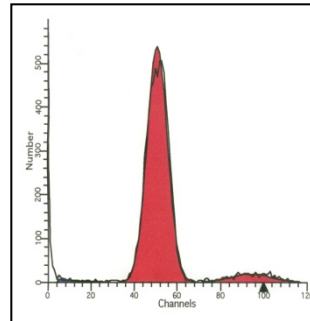
Serial Changes of the DNA histogram after irradiation with 10 Gy of 80 keV/mm carbon beam. (*Tsuboi K: JRR 2007*)

NB1RGB
Normal
Skin fibroblast

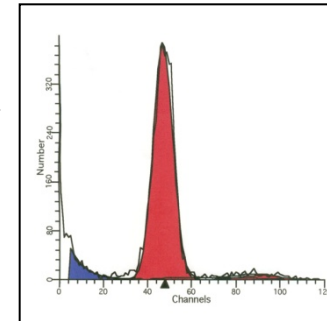
Control



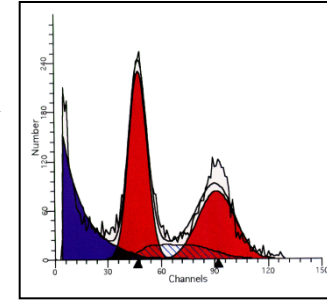
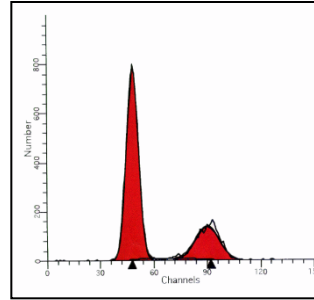
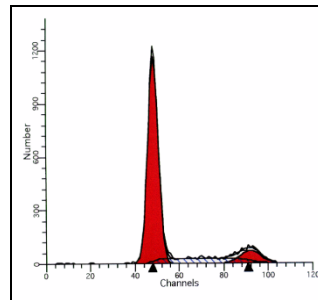
Day 1



Day 7

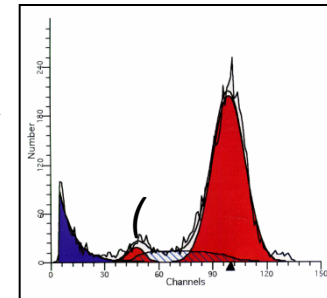
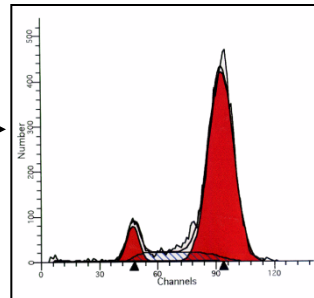
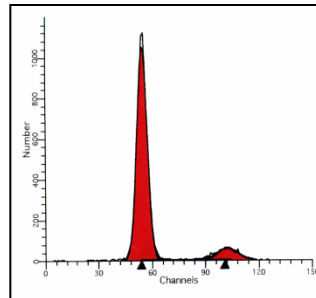


U87MG: P53 +
glioblastoma cell line



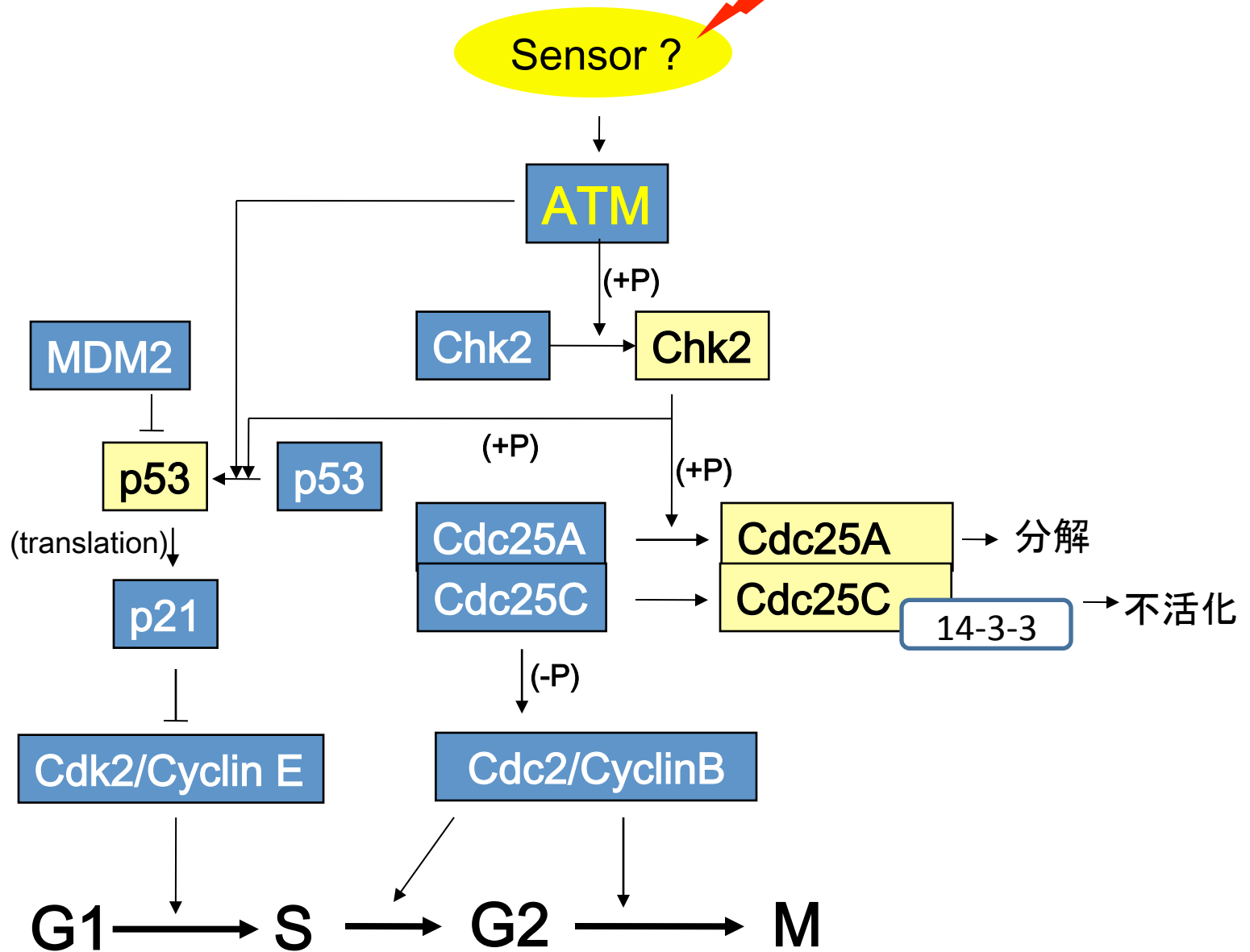
增殖停止

TK1: P53 -
glioblastoma cell line



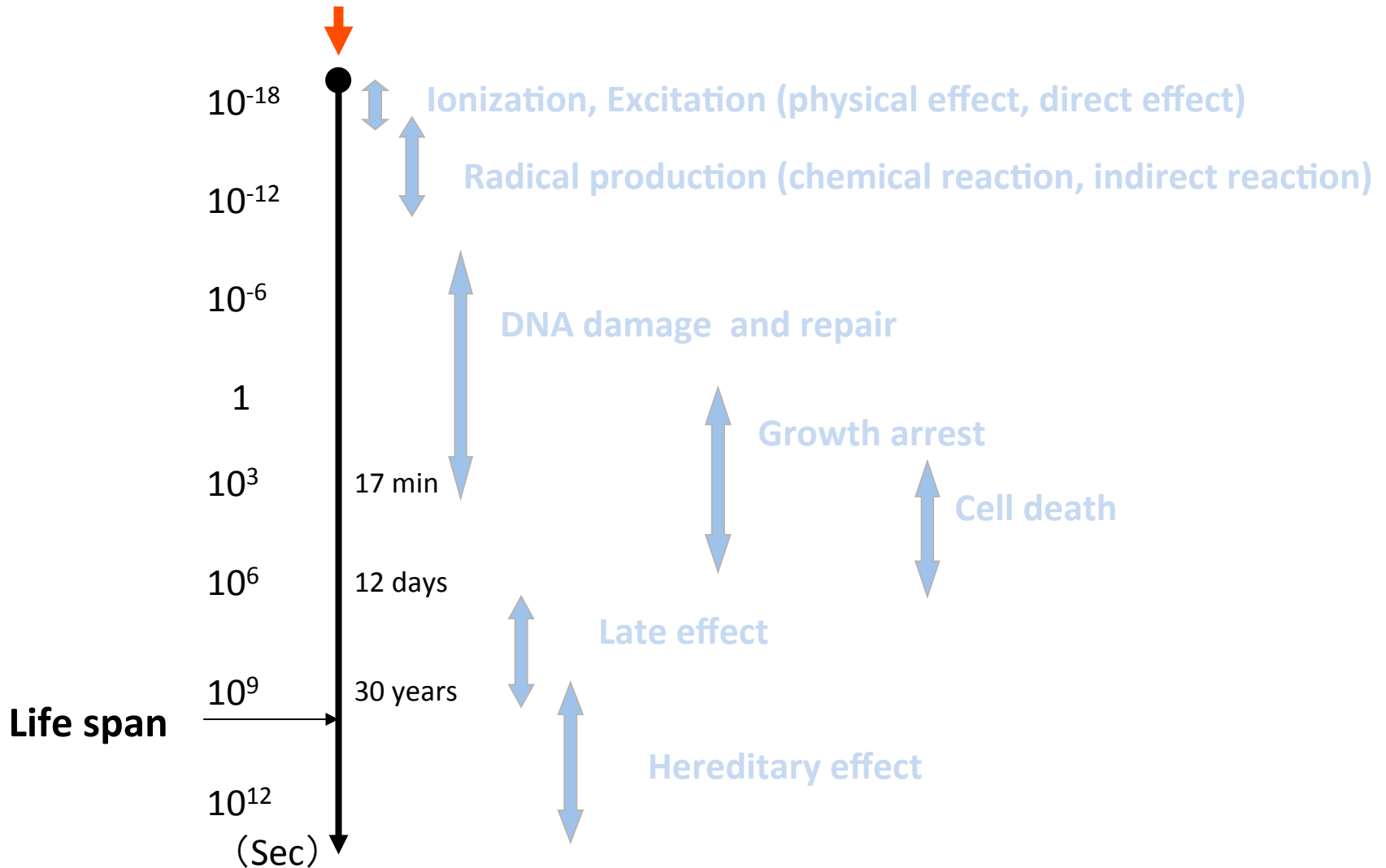
照射後のSignal Transduction

電離放射線



細胞死という現象

Ionizing Radiation



細胞の形態の変化

アポトーシス(apoptosis)

ネクローシス(necrosis)

その他の細胞死

細胞の増殖能の変化

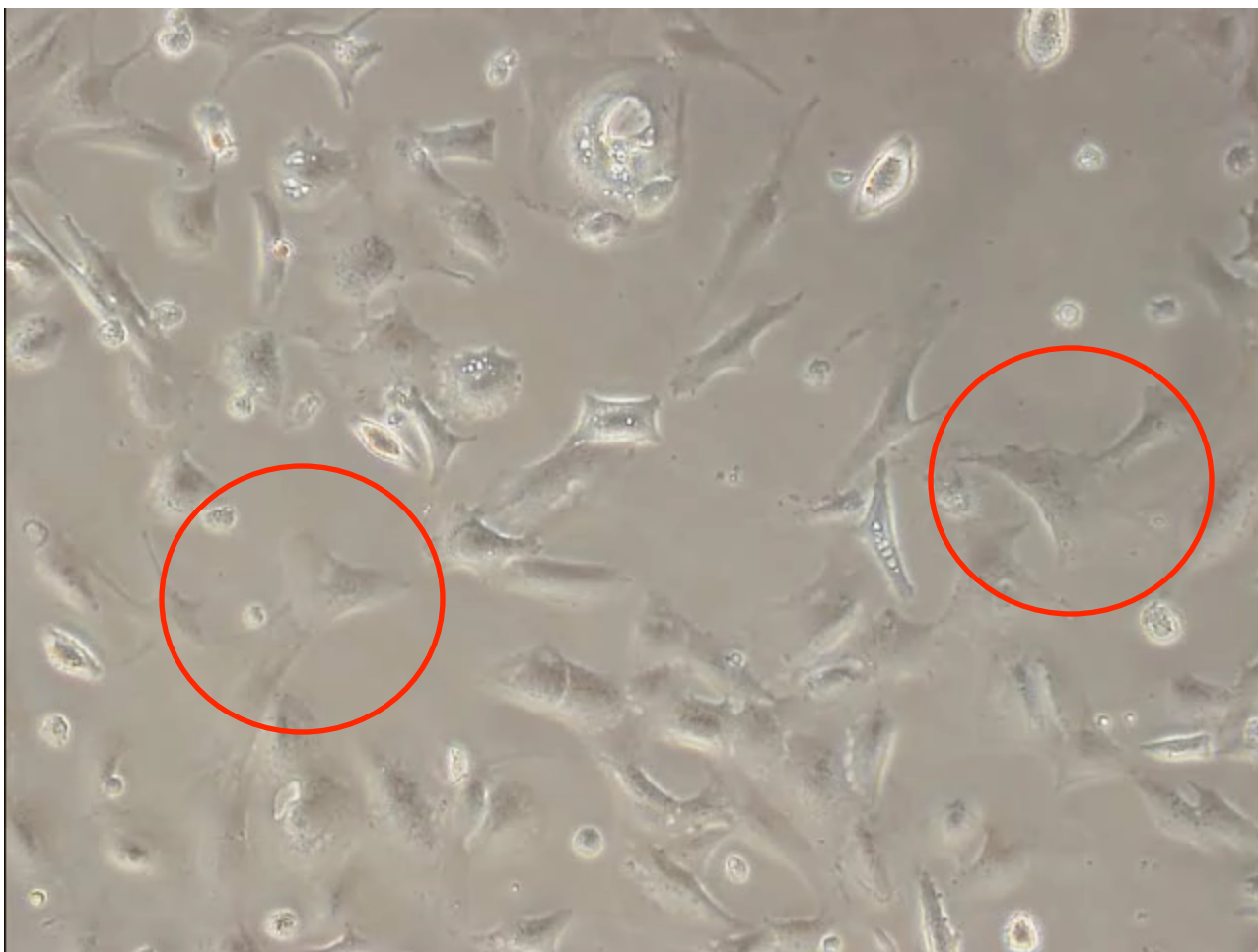
Cell cycle の停止

間期死(interphase death)

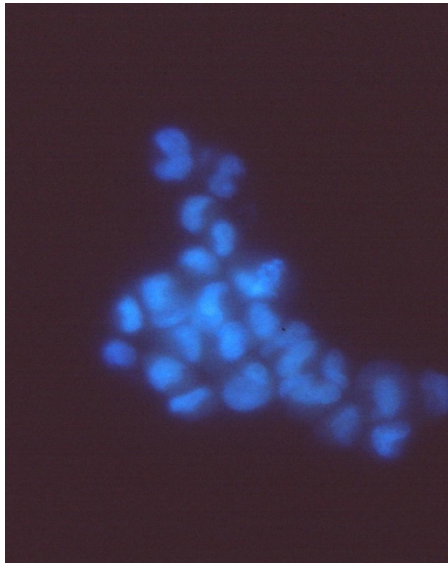
増殖死(reproductive death)

増殖能の消失:

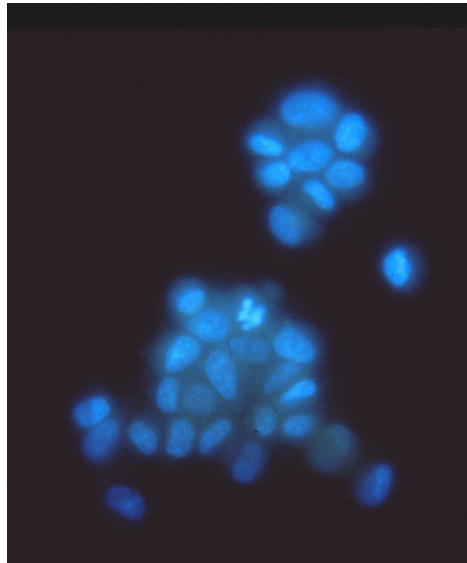
増殖死(Loss of clonogenicity)



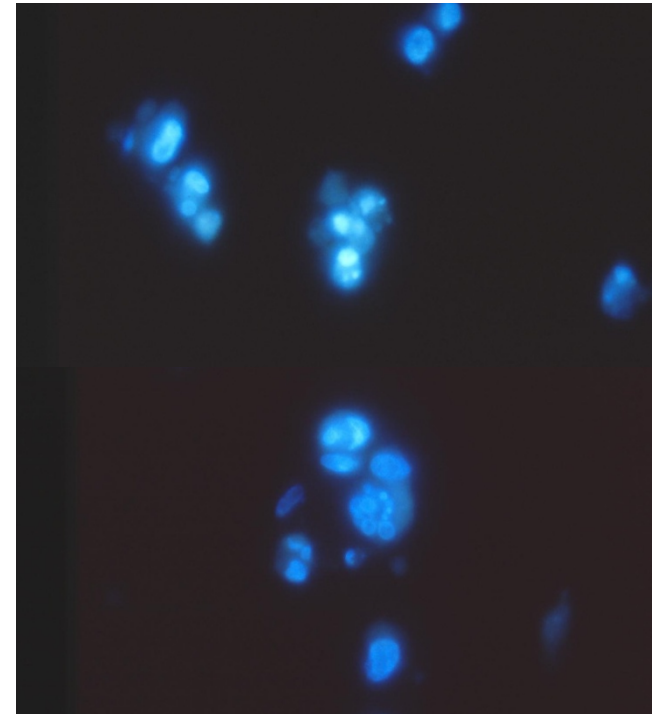
Detection of apoptotic cells by staining with Hoechst 33342 in U87MG cells before and after irradiation with 10 Gy of 80 keV/ μm carbon beam. ($\times 100$)



before



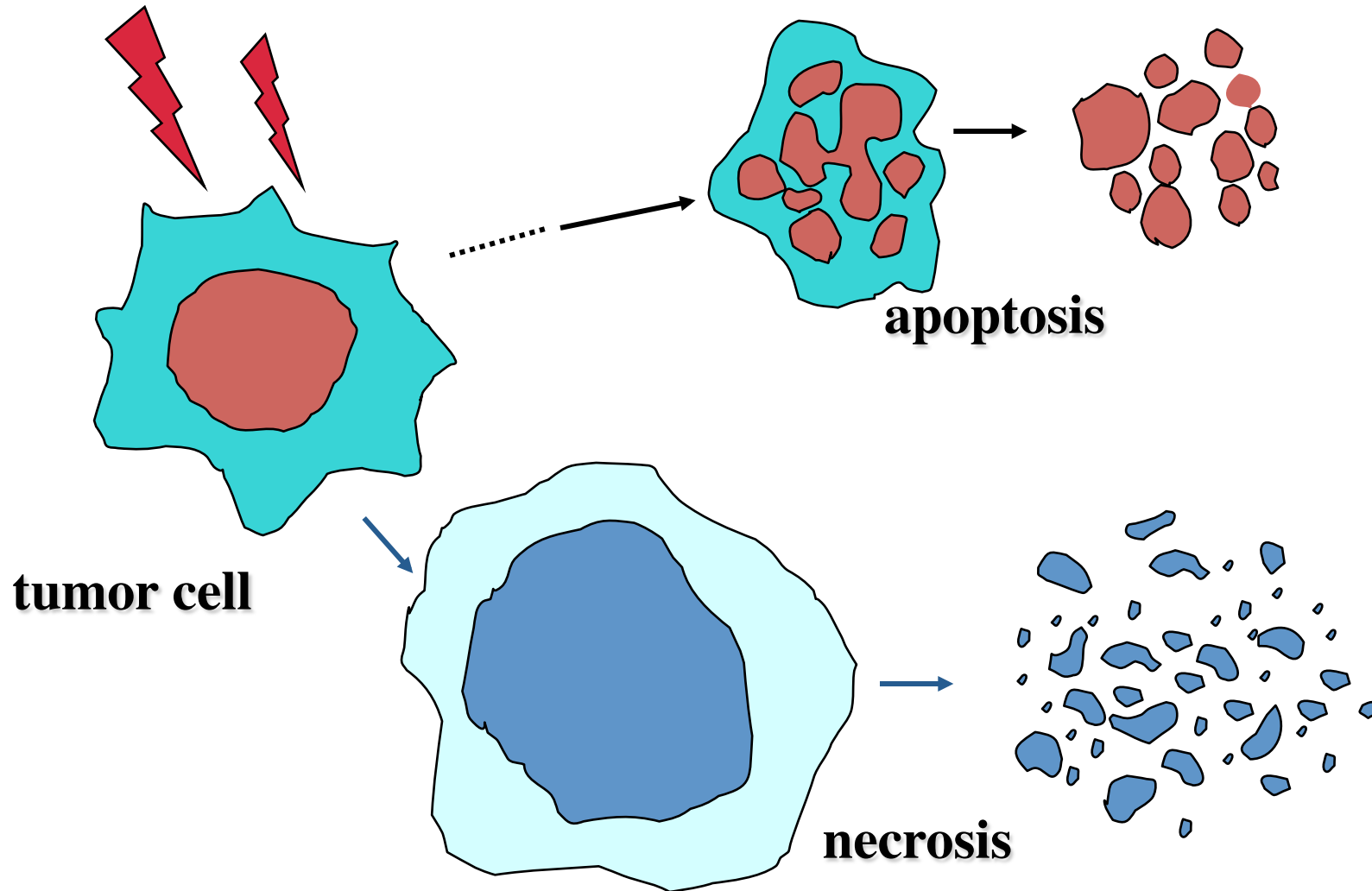
Day 1



Day 7

(Tsuboi K: JRR 2007)

irradiation



細胞死

Apoptosis: プログラムされた細胞の自殺現象、生理的な現象

Chromatin condensation

Nuclear fragmentation

Mediated by **Caspases**

Extrinsic pathway: **FAS, FASL**

Intrinsic pathway: **mitochondria**

Necrosis: 受動的で汚い(messy, dirty)、細胞の自壊現象

Cell swelling

Rupture

Release of intracellular content

Inflammation

電離放射線の生物作用の特徴

- 1) 全ては、エネルギーが水分子かDNAに付与されるという現象から始まる。
- 2) このエネルギー付与はアナログではない。
- 3) デジタル化(量子化)されている。言い換えると、ある塊の単位をもとに反応が起きる。
- 4) その結果、発端となる現象を起こすには分子的にも個体的にも閾値が存在している。
- 5) それを何とか説明するためにヒット論と標的論(hit theory and target theory)が提唱された。
- 6) さらに、それに基づき、線量と反応の関係を説明する数理化モデルが提唱された。

デジタル的に起きる障害と回復という現象

- 非回復性障害

- 致死障害 lethal damage ;(LD)
 - 不可逆性、修復不能、必ず細胞を死に導く損傷

- 回復性障害

- 亜致死障害 sublethal damage ;(SLD)
 - 可逆的で正常な環境下で数時間の内に修復
 - 修復前に別の亜致死損傷が加わり相互作用により致死障害となる
- 潜在的致死障害 potentially lethal damage ;(PLD)
 - 通常的环境下では致死的
 - 照射後の環境により影響を受ける
 - メカニズムについては十分解明されていない

数理化モデル

- 標的説(古典論)

『細胞内に標的、標的がヒット』

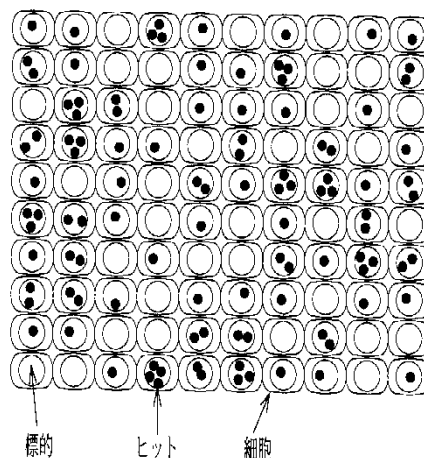
- a) 1標的1ヒットモデル

$$S = \exp(-kD)$$

- b) 多標的1ヒットモデル

$$S = 1 - \{1 - \exp(-D/D_0)\}^n$$

— $D \rightarrow \text{大}; S \doteq n \cdot \exp(-D/D_0)$



- 2(多)要素モデル

— 細胞内には複数種類の標的が存在

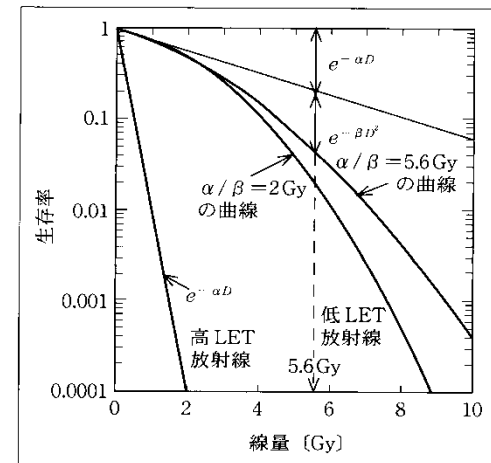
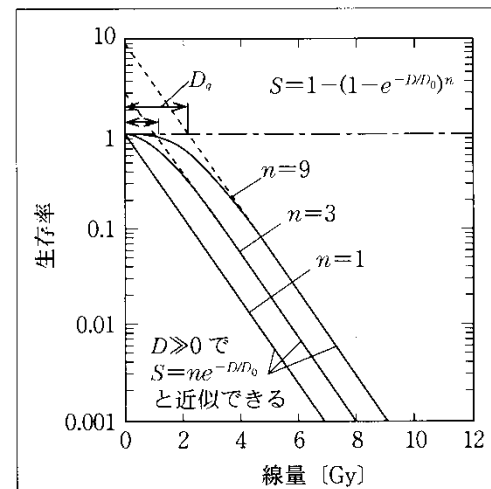
$$S = [\exp(-kD)] \times [1 - \{1 - \exp(-D/D_0)\}^n]$$

- 直線-二次曲線(LQ)モデル

— ミクロな線量分布による解析から

- 1) 複合事象で致死損傷が形成される説
 - 2) 一事象の損傷生成とその回復要因が加わる説

$$S = \exp(-\alpha D - \beta D^2)$$



現在もっとも多く用いられているモデル

標的は2本鎖DNAである。

1粒子(1ヒット)による2本鎖切断と2粒子(2ヒット)による2本鎖切断がある。

1粒子(1ヒット)による2本鎖切断は吸収線量に比例する(一次項: α)と仮定

2粒子(2ヒット)による2本鎖切断は吸収線量の二乗に比例する(二次項: β)と仮定

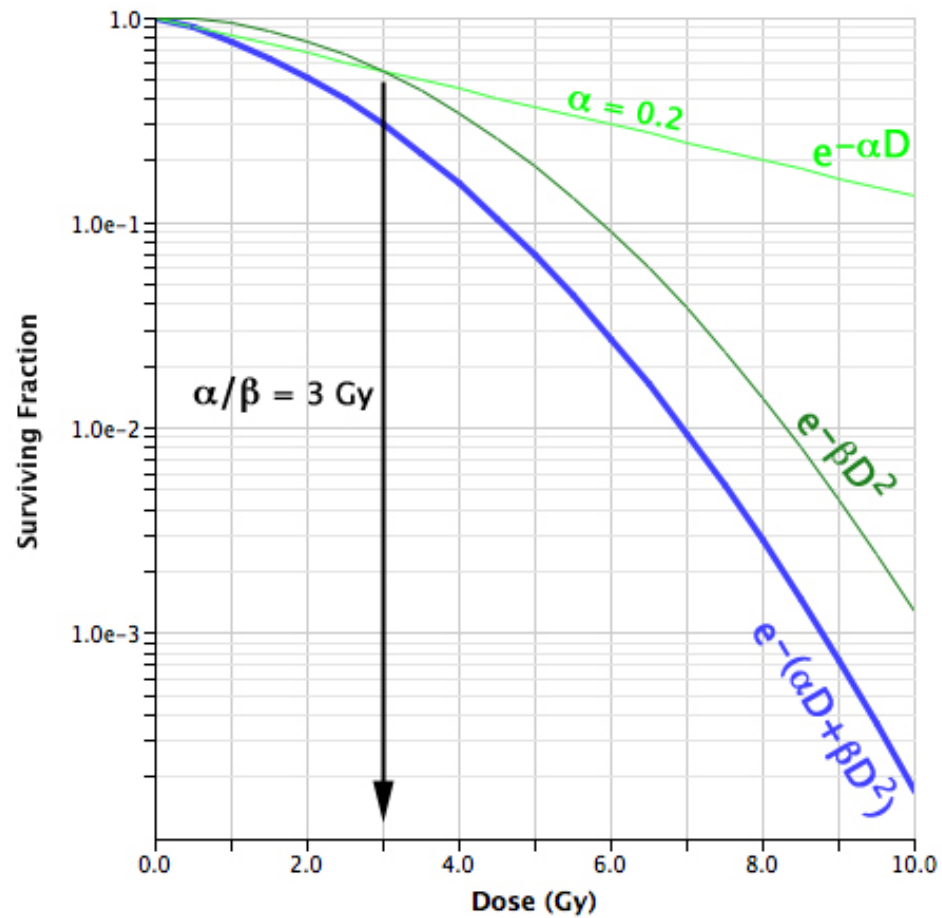
$$I(\text{Incidence}) = \alpha D + \beta D^2$$

$$S / S_0 = e^{-(\alpha D + \beta D^2)}$$

直線-二次曲線(LQ)モデル

組織の反応にも用いられる。

直線-二次曲線(LQ)モデル



放射線に対する
組織や細胞の反応を
どう解析するのか

確定的影響

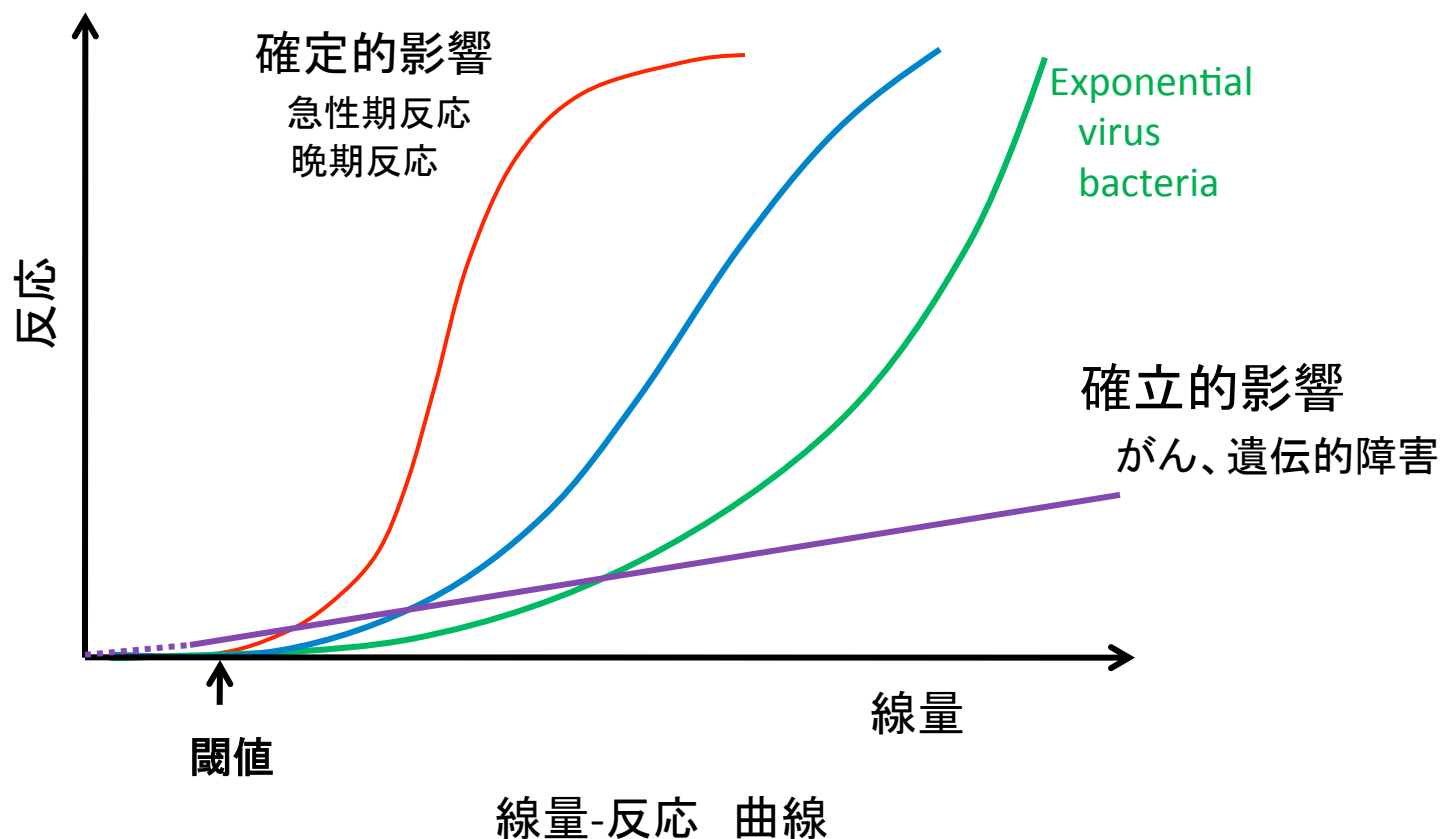
脱毛や不妊など、ある一定の放射線が当たらないと影響が出ないもので、その線量をしきい線量と呼ぶ。

確率的影響

しきい線量がきわめて小さいかなく、低線量から影響が出始めて線量が大きくなるにつれて発生する確率が増える。発がんや遺伝的影響などがこれに分類される。

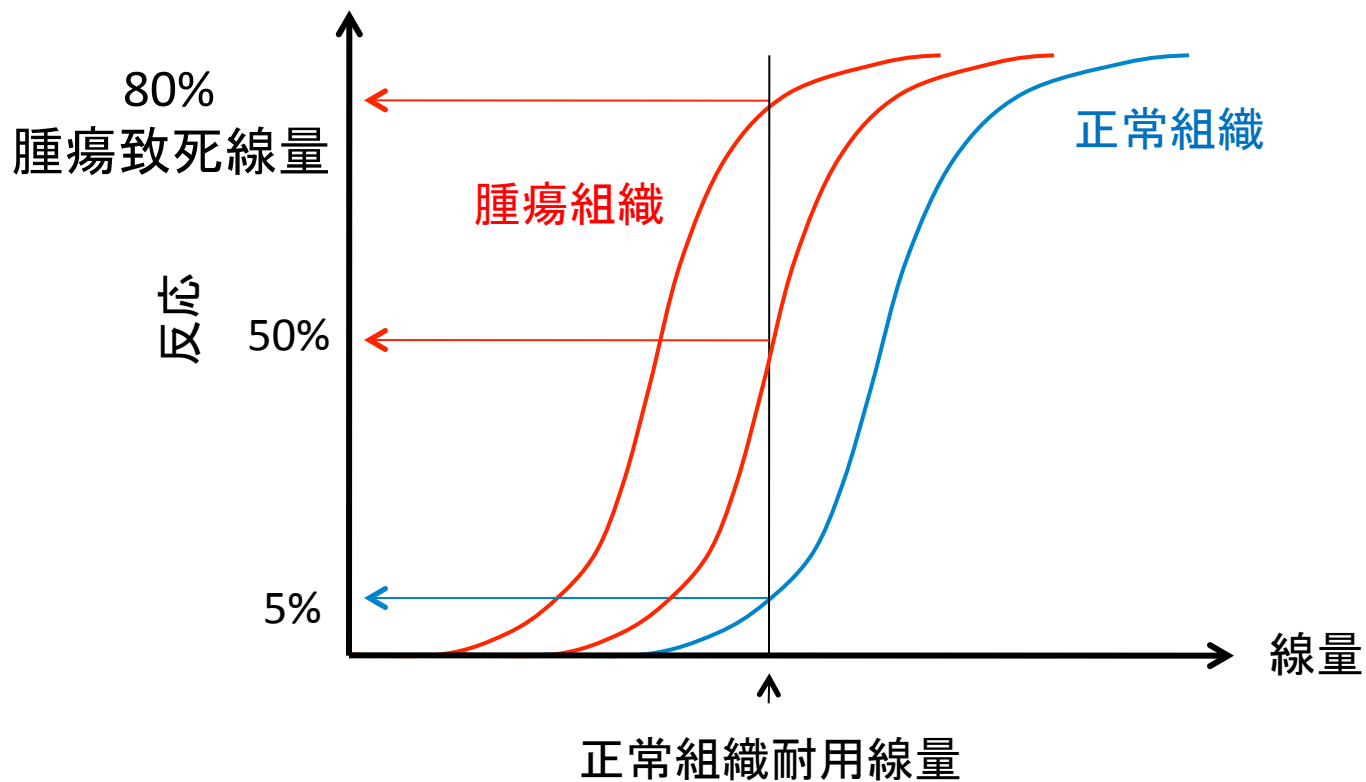
放射線の生物作用の特徴

- 1) 直線的反応
- 2) 指数関数 (exponential)に近い反応
- 3) S字状(sigmoid)の反応



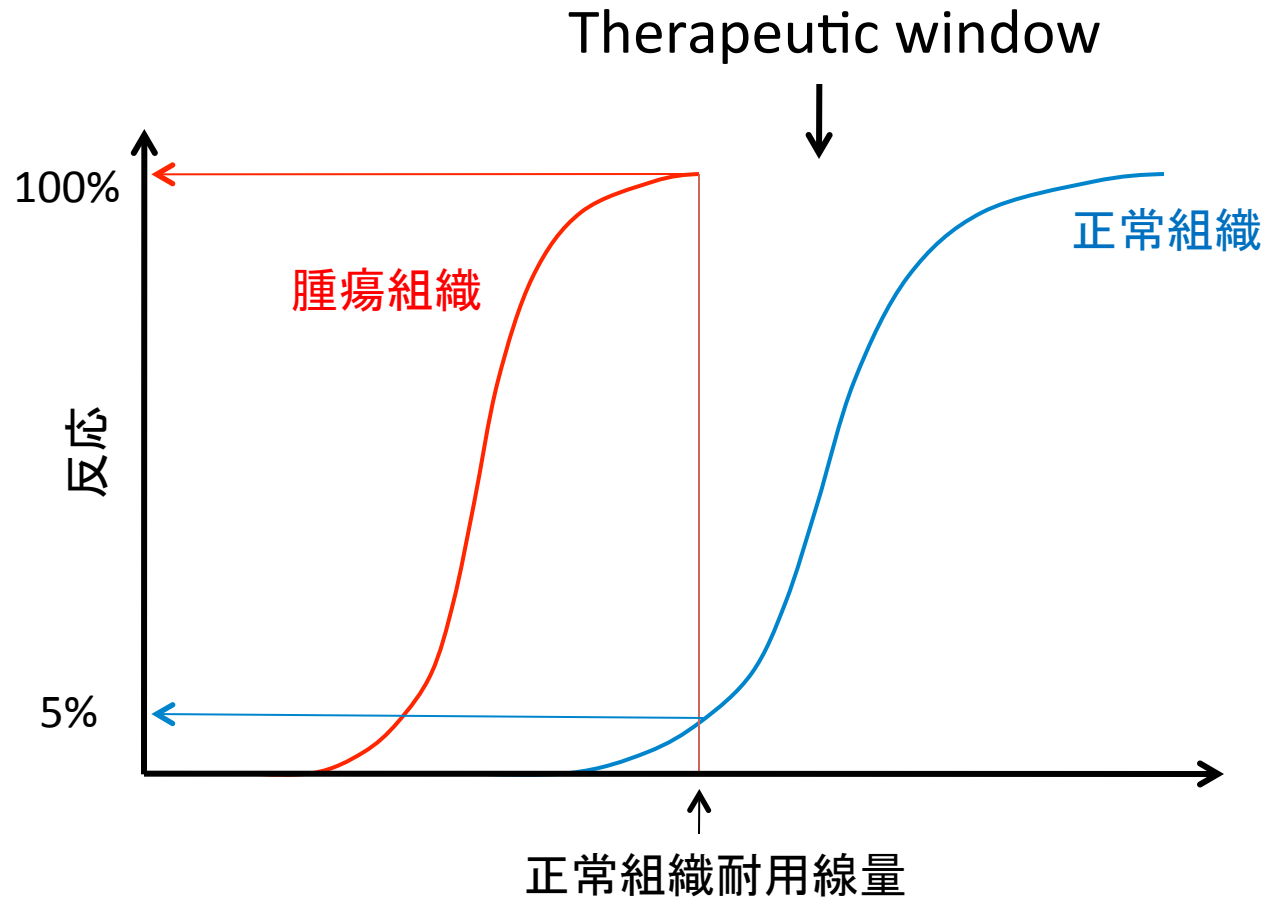
Dose-response curve

線量-反應 曲線



放射線治療に理想的な線量-反応曲線

線質が同じであれば腫瘍組織と正常組織の種類で決まる。



BED: 生物学的等価線量

$$\text{BED} = nd(1+d/\alpha/\beta) \text{ Gy}$$

where “n” is the fractionation number, “d” is the daily dose,
and α/β is assumed to be 10 for tumors and 3 for normal lung
tissue

エックス線に対する正常組織の α/β 値

早期反応

皮膚	9.4-21
毛包(脱毛)	5.5-7.7
口腔粘膜	7.9
大腸	7.1-8.4
睪丸	13.9
脾臓	8.9

晩期反応

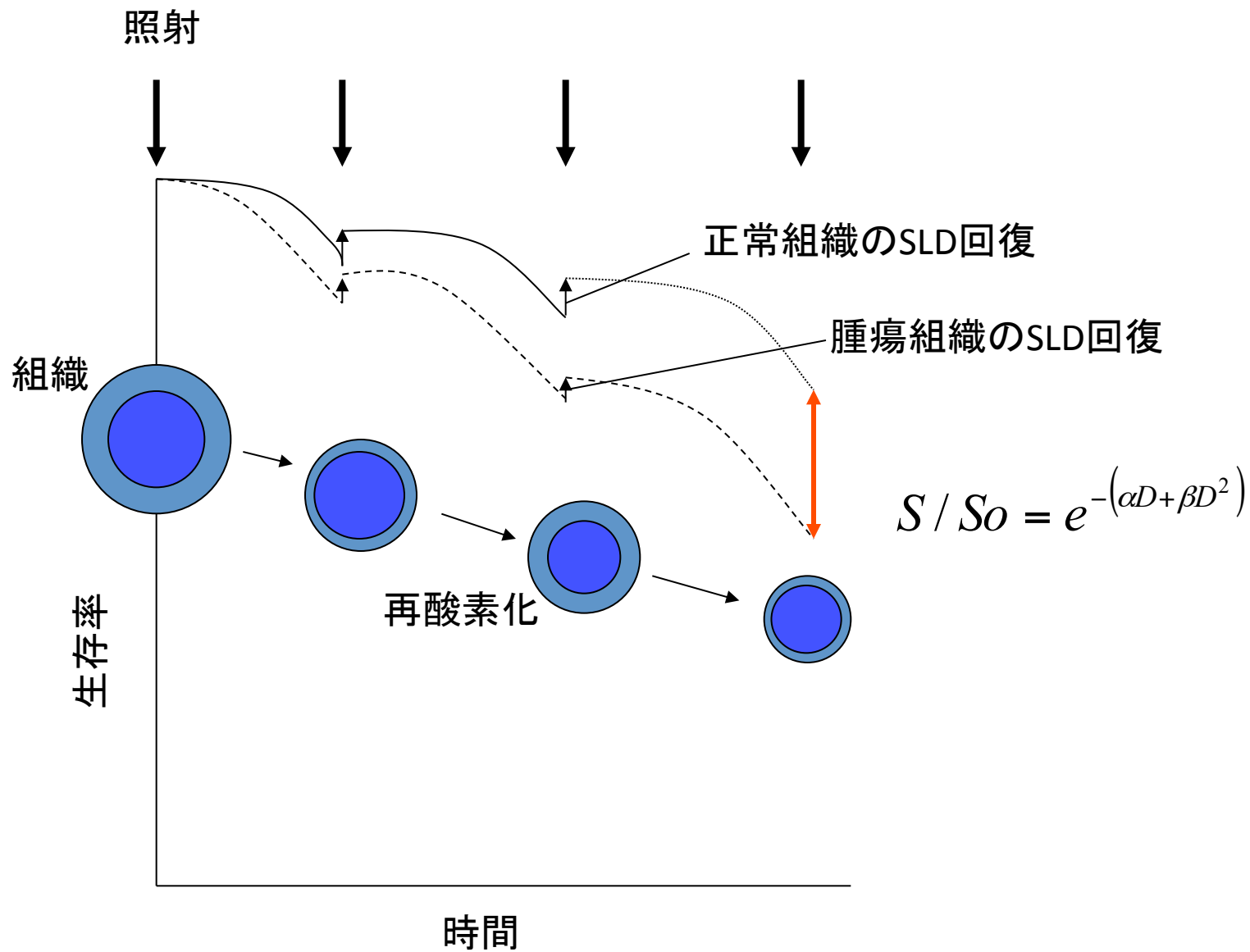
脊髄	2.5-5.2
脳	2.1
口腔粘膜	7.9
眼(白内障)	1.2
肺(肺臓炎)	2.1-4.3
腸	3.0-5.0
皮下組織	1.5

α/β 値が小さいと1回照射の時の生存曲線の肩が大きく曲がる
等効果線量増加は大きくなり、分割効果が表れる(障害は減る)。

α/β 値が大きいと1回照射の時の生存曲線の肩はあまり曲がらない
等効果線量増加は小さく、分割効果は表れにくい(障害は変わらない)。

α/β 値は分割照射効果を知る手がかりとなる。

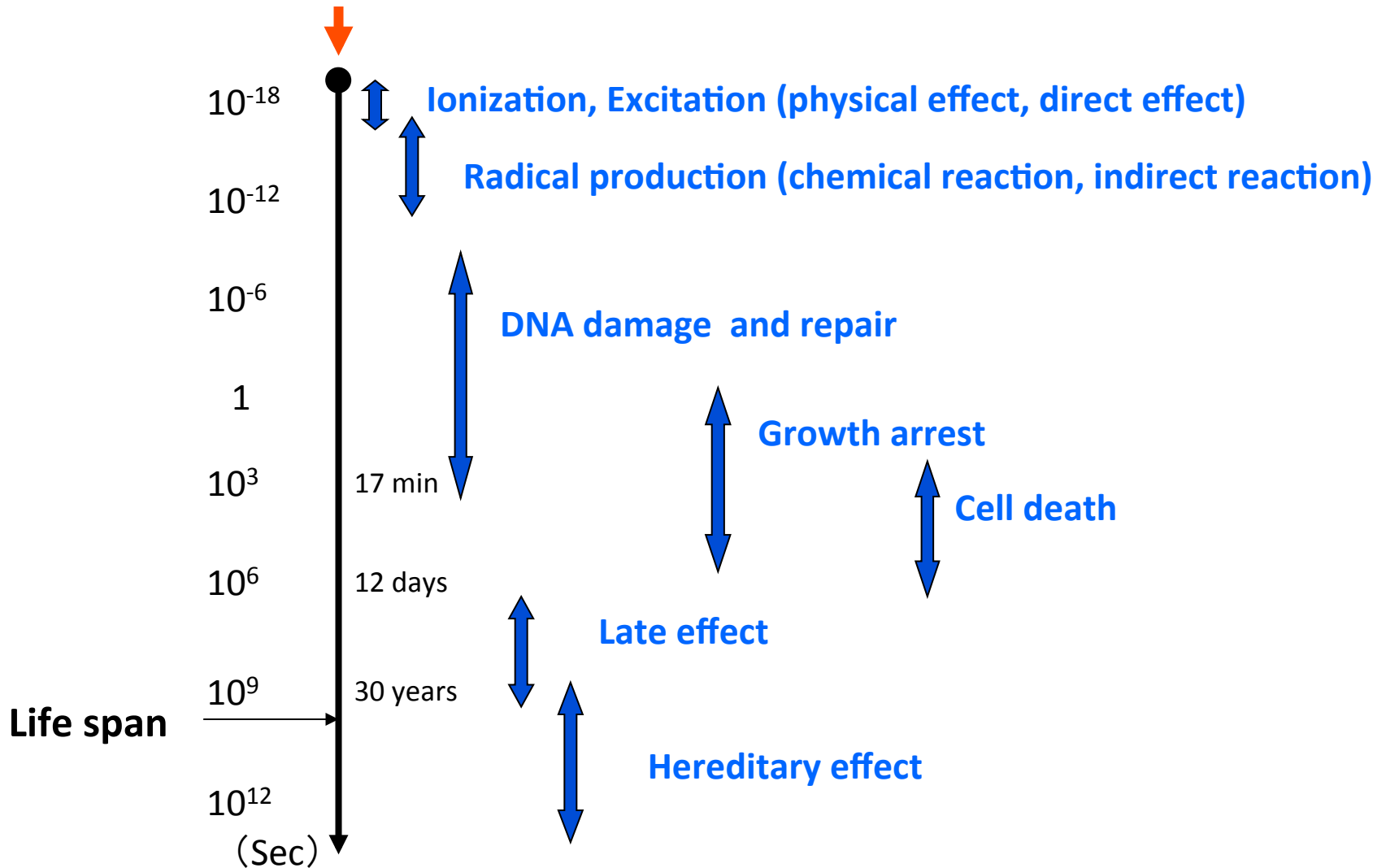
分割照射



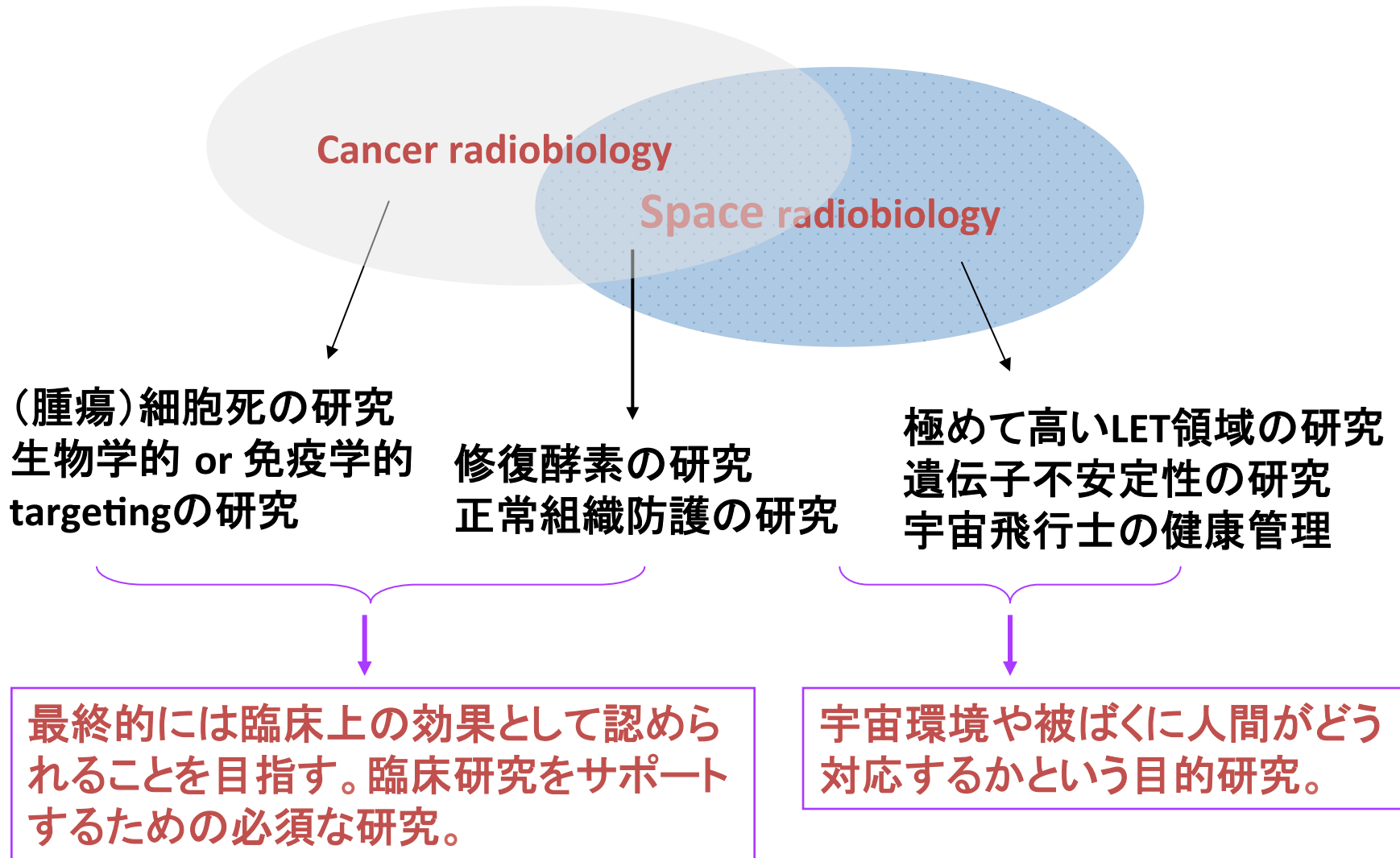
分割照射と4つのR

- Repair(回復): 照射後の細胞のSLD回復
腫瘍 < 正常組織
- Redistribution(再分布): 細胞周期の再分布
- Repopulation(再増殖): 生き残った細胞の再増殖
腫瘍 < 正常組織
- Reoxygenation(再酸素化): 酸素濃度の高い細胞が先に死んだ後の血流の回復

Ionizing Radiation



放射線生物学



今日の目的は達成されたか？

放射線がどのようにして細胞に影響を及ぼすのかを理解する。

放射線に対して組織はどのように反応するのかを理解する。

がん治療における放射線治療の理論