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CHROMOSOME HETEROMORPHISMS IN THE JAPANESE

I. BANDING PATTERNS OF Dp+ AND Gp+ BY Q- AND C-STAINING METHODS

日 本 人 に お け る 染 色 体 の 異 形 性

I. Q-お よ び C-染 色 法 に よ る Dp+ と Gp+ の 分 染 パ タ ー ン

TOSHIO SOFUNI, Sc.D. 祖父尼俊雄
KAZUMI TANABE 田辺和美
AKIO A. AWA, Sc.D. 阿波章夫

放影研
RERF

RADIATION EFFECTS RESEARCH FOUNDATION
財団法人 放 射 線 影 響 研 究 所

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CHROMOSOME HETEROMORPHISMS IN THE JAPANESE
I. BANDING PATTERNS OF Dp+ AND Gp+ BY Q- AND C-STAINING METHODS

日本人における染色体の異形性
I. Q-およびC-染色法によるDp+とGp+の分染パターン

TOSHIO SOFUNI, Sc.D. (祖父尼俊雄); KAZUMI TANABE (田辺和美);
AKIO A. AWA, Sc.D. (阿波章夫)

Department of Clinical Laboratories
臨床検査部

SUMMARY
Thirty-four cases with Dp+ and Gp+, known to be chromosome heteromorphisms in man, were examined using Q- and C-staining methods. Of 18 cases with Dp+, 14 involved No.15 chromosome and 2 each were No.13 and No.14 respectively. Of 16 cases with Gp+, 13 were concerned with No.22 and the remaining 3 were No.21. Short arm regions of eight cases with 15p+ and one with 14p+ were stained very darkly by the C-method, but did not fluoresce brilliantly by the Q-method. On the other hand, brightly fluorescing short arm regions observed in three cases with 15p+ and two with 22p+, were not very darkly stained by the C-method. In the remaining 20 cases, short arm regions were not stained positively by either method, but showed negatively or intermediately variable staining intensities.

INTRODUCTION
It is well-known that short arms and satellites of human acrocentric chromosomes vary considerably, and that these chromosome variants have been found in a large number of individuals, most of whom are phenotypically normal. Recently developed banding techniques offer opportunities to determine a more precise definition of variant chromosomes, and also to identify additional new chromosome variants hitherto undetected by conventional staining methods.[1-5]

In the present study, D or G chromosomes with an enlarged short arm (Dp+ or Gp+) detected by

要 約
ヒトの染色体異形として知られているDp+およびGp+34例について，Q-とC-染色法を用いて分染パターンを比較した．18例のDp+のうち14例がNo. 15で，No. 13とNo. 14は2例ずつあった．16例のGp+のうち13例がNo. 22で，残り3例がNo. 21であった．14p+の1例と15p+の8例では短腕がC-法で非常に濃く染まったが，Q-法では強く光らなかった．一方，15p+の3例と22p+の2例では短腕はQ-法で強く光ったが，C-法による非常に濃い染色性はみられなかった．残りの20例はすべて両法で濃染されず，微細な分染パターンの変異がみられた．

緒 言
ヒトの端部着糸型染色体の短腕と付随体にかなりの変異がみられることはよく知られており，しかもこれらの染色体変異は多数の人々にみいだされ，それらの多くは表現型が正常である．近年開発された分染法によって変異染色体をより正確に分類することができるとともに，通常の染色法ではこれまで識別できなかった新しい染色体変異を識別することも可能となった．[1-5]

本調査においては通常法によってみいだされた大きな短腕をもつDあるいはG染色体(Dp+あるいはGp+)

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the conventional method in 34 individuals, were also examined using Q- and C-staining methods. Detailed banding patterns of the enlarged short arm of these variant chromosomes are presented.

MATERIALS AND METHODS

The individuals studied were selected from among participants of the RERF Adult Health Study (AHS) sample and the F_1 Mortality Study (F_1) sample in Hiroshima. The former comprises atomic bomb survivors and nonexposed control subjects, and the latter consists of the offspring born to the exposed parents and their controls. The characteristics of both samples have been described elsewhere.[6,7] In the course of studies of chromosome heteromorphisms in both samples, about 40 individuals with a D or G chromosome having an enlarged short arm (Dp+ or Gp+) were detected by the conventional staining method, and 34 of them were successfully examined using both Q- and C-staining method. In 13 cases from the AHS sample, no physical or phenotypic abnormalities were observed in clinical examination at RERF. No clinical examination was performed for the F_1 sample members, unless they requested it; however, in none of the 21 offspring with chromosome variants was any unusual phenotype noted during an interview by well-trained nurses while answering a questionnaire dealing with marital status, individual family and health histories, and similar matters.

Chromosome preparations were made from whole blood culture by the routine air-dry method. The Q-banding patterns were obtained by a slightly modified technique of Caspersson et al,[8] and the C-staining analysis was carried out according to the method of Sumner.[9] All individuals were examined independently by the conventional, Q- and C-staining methods. In addition, successive staining was carried out on the same metaphases in combination with either Q- and conventional methods, or Q- and C-methods, and identification of variant chromosomes and banding patterns of their enlarged short arm were confirmed.

Morphological criteria for Dp+ and Gp+ detected by the conventional method are as follows: Enlarged short arms of D and G chromosomes are approximately twice as large as the next largest short arms of any chromosomes in the group concerned, that is, almost equal to or

の34例についてQ-およびC-染色法を用いて分析した．これら変異染色体の大きい短腕の分染パターンについて詳細に述べる．

材料および方法

調査対象者は広島における放影研成人健康調査集団（AHS）とF_1寿命調査集団（F_1）である．前者は原爆被爆者と非被爆対照者から成り，後者は被爆者および対照者の子供たちである．両対象集団の特徴については別に報告している．[6,7] 両集団において染色体の異形性について通常法を用いて調べたところ，およそ40例に大きな短腕をもつDあるいはG染色体（Dp＋あるいはGp＋）がみつかり，これらのうち34例についてQ-とC-染色法を用いて分析することができた．成人健康調査集団の13例については，放影研における臨床診察からは身体的異常や表現型異常は認められなかった．F_1集団対象者では，特に要望がないかぎり臨床診察は行われていない．しかし，F_1集団の染色体変異21例については熟練した看護婦が質問票に婚姻，家族，健康，その他について記入する際に表現型異常を認めていない．

染色体標本は全血培養後に通常の空気乾燥法を用いて作製した．Q-分染パターンは若干の改変を加えたCaspersson ら[8]の方法を用い，C-染色法による分析はSumner [9]の方法に従った．通常の染色法，Q-およびC-染色法は全例について別々に行った．さらに同一の中期分裂像についてQ-および通常染色法，あるいはQ-およびC-染色法を併用し，変異染色体の同定と大きな短腕の分染パターンの確認を行った．

通常染色法によるDp＋とGp＋の形態的な基準は次の通りである：DおよびG染色体の短腕が同一グループ内の二番目に大きい短腕の約2倍，すなわち

larger than the short arm of No.17 chromosome. No distinct secondary constriction was observed in any case studied, though their enlarged short arms were occasionally stained faintly.

The staining intensity by the Q-method was described according to the definition of the Paris Conference Supplement.[10] The approximate intensity by the C-method was classified into the following five groups; 5: very dark intensity equal to "C-band", 4: darker intensity than that of the euchromatic region, 3: intermediate intensity similar to the euchromatic region, 2: lighter intensity than that of the euchromatic region, 1: negative intensity. The term "C-band" is used here to describe a unit of constitutive heterochromatin stained by the C-method according to the nomenclature of the Paris Conference.[11]

RESULTS

Of 34 cases studied, 18 were found to be Dp+ and 16 were Gp+. Six cases with Dp+ and 7 with Gp+ were found in the AHS sample, while in the F_1 sample 12 with Dp+ and 9 with Gp+ were observed. Results on the frequencies in both samples of these variants will be reported elsewhere.

Analyses of Q-banding patterns indicated that one of No.15 chromosomes was found to have an enlarged short arm in 14 cases with Dp+, and one of No.13 and No.14 chromosomes were identified as the variant chromosome in each of 2 cases (Table 1). Out of 16 cases with Gp+, 13 had a No.22 chromosome with an enlarged short arm, and 3 were found to be 21p+.

The staining intensity of the enlarged short arm by Q- and C-methods was found to show a lack of uniformity along the entire length and frequently differed among proximal, middle and distal regions. Therefore, the description is made to approximate intensity of these three regions of the enlarged short arm (Table 1). In all cases studied, a very dark band stained by the C-method, or a C-band, was recognized on the proximal region of the enlarged short arm. By the Q-method, the proximal region in all cases showed pale fluorescence, except for one of the cases with 13p+ having a brilliant proximal region similar to the brilliant short arm frequently observed in the normal No.13 chromosomes (Figure 1).

No. 17染色体の短腕にほぼ等しいかそれより大きいものである．大きい短腕は時折薄く染まることはあるが，明瞭な二次狭窄は全例において認められなかった．

Q-法による染色の強さはパリ会議補遺[10]の定義に従って記述した．C-法による染色の強さはほぼ次のように五つのグループに分類した．5：" C-バンド "と等しく非常に濃い，4：真正染色質部位より濃い，3：真正染色質部位と同じく中程度，2：真正染色質部位より薄い，1：全く染色されない．ここで用いている" C-バンド "はパリ会議[11]の命名法に従ってC-法で濃染する構造性異質染色質を示している．

結　果

調査した34例のうち18例は Dp＋で16例は Gp＋であった．成人健康調査集団には Dp＋が6例，Gp＋が7例みつかり，一方F_1集団には Dp＋が12例，Gp＋が9例みつかっている．両集団におけるこれらの変異体の出現頻度については別に報告する予定である．

Q-分染パターンの分析から，Dp＋のうち No. 15染色体の短腕の大きい例が14例あることが判明し，変異染色体が No. 13と No. 14染色体であったのはそれぞれ2例ずつあった（表1）．16例の Gp＋のうち，13例は No. 22の短腕が大きく，残りの3例は21p＋であった．

大きな短腕における Q-と C-法の染色性は短腕全体にわたって一様でなく，しばしば基部，中間部，端部において異なっていた．それ故，大きい短腕の染色性についてはこれら三つの部位に分けて記述した（表1）．調査した全例において C-法で非常に濃く染まるバンド，すなわち C-バンド，が大きい短腕の基部にみられた．この基部は Q-法では全て淡く光るが，例外として13p＋の1例では基部が強く光った．これは正常の No. 13染色体に時折みられる強く光る短腕と同じである（図1）．

TABLE 1 STAINING INTENSITY* OF PROXIMAL, MIDDLE, AND DISTAL REGIONS OF ENLARGED SHORT ARM BY Q- AND C-METHODS IN 34 CASES WITH Dp+ AND Gp+

表1　34例のDp＋とGp＋の大きな短腕の基部，中間部，端部のQ-法とC-法による染色性*

Variant	Sample	MF No.	Sex	Age	Proximal		Middle		Distal	
					QFQ	CBG	QFQ	CBG	QFQ	CBG
13p+	F_1	[redacted]	F	28	5	5	1	4	2	4
	AHS		M	47	2	5	4	4	2	4
14p+	F_1		F	25	2	5	1	5	2	5
			M	26	2	5	1	2	2	2
15p+	F_1		M	29	2	5	5	4	5	4
			M	19	2	5	5	4	5	4
			M	26	2	5	5	4	5	4
	AHS		M	42	2	5	3	5	3	5
	F_1		F	24	2	5	3	5	2	5
			M	21	2	5	2	5	3	5
			F	19	2	5	2	5	2	5
			F	29	2	5	2	5	2	5
	AHS		F	44	2	5	3	5	2	2
			F	41	2	5	3	5	2	2
			F	66	2	5	2	5	2	2
	F_1		F	20	2	5	3	4	3	4
	AHS		M	83	2	5	1	2	2	2
	F_1		F	21	2	5	1	2	2	2
21p+	AHS		F	64	2	5	3	4	5	3
			M	42	2	5	1	3	5	4
	F_1		F	21	2	5	1	3	5	4
22p+	AHS		F	48	2	5	5	3	5	3
	F_1		M	26	2	5	5	3	5	3
			M	22	2	5	1	4	2	4
			F	25	2	5	1	4	2	4
			F	19	2	5	1	3	3	3
	AHS		F	41	2	5	1	2	3	3
	F_1		F	29	2	5	1	2	3	3
			F	22	2	5	1	2	3	3
	AHS		F	49	2	5	1	2	3	2
	F_1		F	26	2	5	1	2	3	2
			F	20	2	5	1	2	3	2
	AHS		M	46	2	5	1	2	2	3
			M	73	2	5	1	2	2	3

*See text. QFQ: Q-bands by fluorescence using quinacrine. CBG: C-bands by barium hydroxide using Giemsa.

As shown in Table 1, the staining intensity of the middle and distal regions of the enlarged short arms was found to be very variable from case to case. The brilliantly fluorescing middle and distal regions were observed in three cases with 15p+ and two with 22p+, and their C-staining intensity was dark or intermediate (Figures 2 and 3). On the other hand, the entire short arms of one case with 14p+ and five with 15p+ were stained very dark by the C-method, and

表1に示してあるように，大きい短腕の中間部と端部の染色性は個体によってかなりの変異がみられた．15p＋の3例と22p＋の2例において中間部と端部がQ-法で強く光るが，C-法では濃くあるいは中程度に染まった（図2と3）．一方，14p＋の1例と15p＋の5例では短腕全体がC-法で非常に濃く染まったが，Q-法では中程度あるいは淡く光り，例外として14p＋

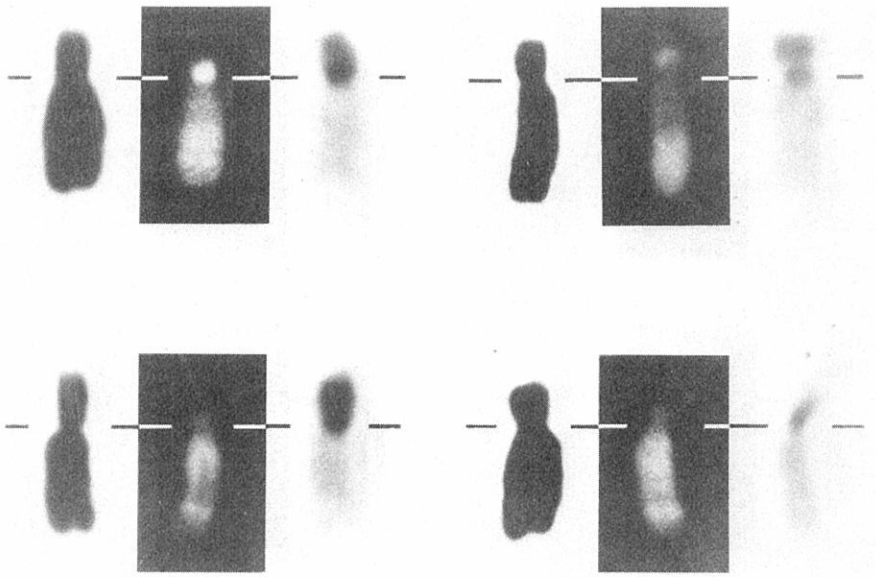

Figure 1. Variant chromosomes of two cases with 13p+ (upper row) and two with 14p+ (lower row) stained by the conventional (left), Q- (center), and C- (right) methods.

図1．通常法（左側），Q-法（中央），C-法（右側）で染色した2例の13p＋（上段）と2例の14p＋（下段）の変異染色体

with intermediate to pale fluorescence by the Q-method, except for negative fluorescence in middle region of the case with 14p+ (Figures 1 and 2). Almost identical banding patterns were observed in three additional cases with 15p+: only the light intensity in their distal region by the C-method differed from that of the above five cases with 15p+ (Table 1).

In three cases, one each with 13p+, 15p+, and 21p+, the fluorescence of the middle and distal regions was intense to pale by the Q-method and stain by the C-method was dark to light, except for brilliant fluorescence in the distal region of the case with 21p+ (Figures 1-3). In the remaining 17 cases, consisting of one each with 13p+ and 14p+, 2 each with 15p+ and 21p+, and 11 with 22p+, the middle region was characterized by negative fluorescence by the Q-method. Though the distal region of two cases with 21p+ fluoresced brilliantly, the other cases showed an intermediate or pale fluorescence of the distal region. By the C-method, the staining of the middle and distal regions in these cases was dark to light.

の中間部だけは全く染まらなかった（図1，2）．さらに15p＋の3例においてもほぼ同じような分染パターンが得られた：端部がC-法で薄く染まる点だけが上述の15p＋の5例とは異なっていた（表1）．

13p＋，15p＋，21p＋，それぞれ1例ずつ，計3例においては中間部と端部がQ-法によって明るく光るものから淡く光るものまでみられ，C-法によっても濃く染まるものから薄く染まるものまであった．例外として21p＋の端部は強く光っていた（図1－3）．残り17例は13p＋と14p＋がそれぞれ1例ずつ，15p＋と21p＋が2例ずつ，22p＋が11例あったが，これらの中間部はQ-法によって全く染まらないという特徴があった．21p＋の2例の端部は強く光っていたが，他の端部は全て中程度あるいは淡く光っていた．C-法ではこれらの中間部と端部は濃く染まるものから薄く染まるものまでみられた．

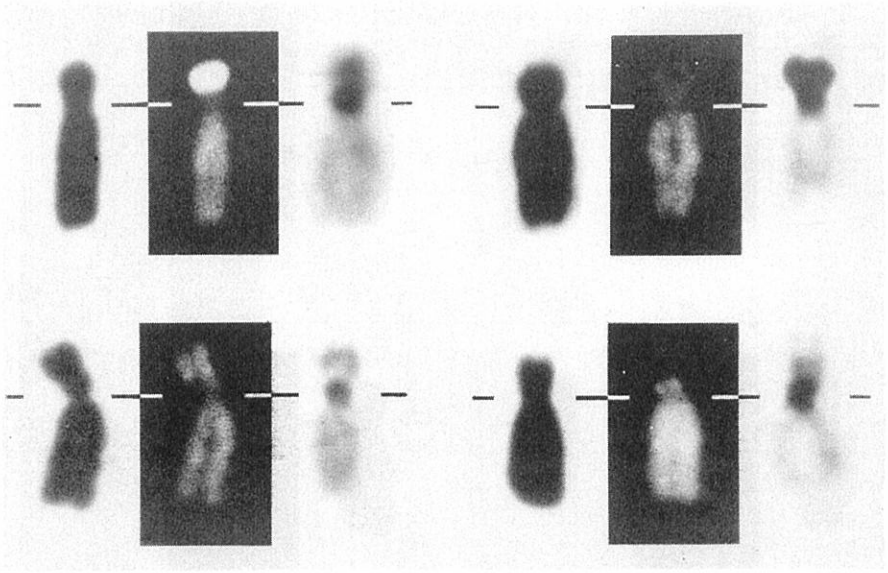

Figure 2. Variant chromosomes of four representative cases with 15p+ stained by the conventional (left), Q- (center), and C- (right) methods.

図2．通常法（左側），Q-法（中央），C-法（右側）で染色した代表的な4例の15p＋の変異染色体

The above findings indicate that the banding patterns of the enlarged short arm of Dp+ and Gp+ vary markedly among cases, and that even the regions with identical fluorescence intensity by the Q-method frequently showed different intensities by the C-method, or vice versa.

To further clarify the relationships of these variable banding patterns, the Dp+ and Gp+ were temporarily classified into five types based solely on the staining intensity of the middle region of the enlarged short arm (Figure 4). Type 1: The middle region having brilliant fluorescence by the Q-method and dark intensity by the C-method. Type 2: The middle region with intermediate or pale fluorescence, but very dark intensity by the C-method. Type 3: The fluorescence of middle region was intense to pale by the Q-method, and stain by the C-method was dark to light. Type 4: The negatively fluorescing middle region by the Q-method was stained very dark by the C-method. Type 5: The middle region stained negatively by the Q-method and stain by the C-method was dark to light.

上述の結果はDp＋とGp＋の大きな短腕の分染パターンには著しい変異のあることを示しており，Q-法で同じような染色性を示す部位でもC-法では異なる染色性を示したり，またその逆の染色性を示すこともあった．

これら分染パターンの多様性をさらに明確にするために，大きな短腕の中間部だけの染色性を基にしてDp＋とGp＋を便宜的に五つのタイプに分類した（図4）．タイプ1：中間部がQ-法で強く光り，C-法で濃く染まる．タイプ2：中間部がQ-法で中程度あるいは淡く光り，C-法で非常に濃く染まる．タイプ3：中間部がQ-法で明るく，中程度あるいは淡く光り，C-法でも濃く，中程度あるいは薄く染まる．タイプ4：Q-法で中間部は全く染まらないが，C-法で非常に濃く染まる．タイプ5：中間部はQ-法で全く染まらず，C-法では濃く，中程度あるいは薄く染まる．

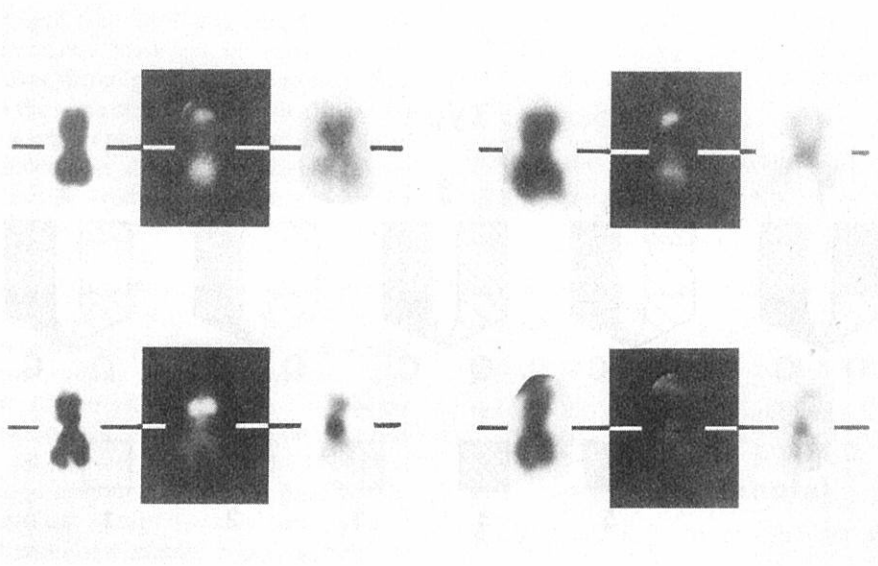

Figure 3. Variant chromosomes of two cases with 21p+ (upper row) and two representative cases with 22p+ (lower row) stained by the conventional (left), Q- (center), C- (right) methods.

図3．通常法（左側），Q-法（中央），C-法（右側）で染色した2例の21p＋（上段）と代表的な2例の22p＋（下段）の変異染色体

TABLE 2 NUMBER OF CASES WITH Dp+ AND Gp+ CLASSIFIED BY INTENSITY OF MIDDLE REGION OF ENLARGED SHORT ARM

表2　大きな短腕の中間部の染色性によって分類したDp＋とGp＋の例数

Type	Intensity*		Chromosome number					Total
	QFQ	CBG	13	14	15	21	22	
1	5	2-4	0	0	3	0	2	5
2	2-4	5	0	0	8	0	0	8
3	2-4	2-4	1	0	1	1	0	3
4	1	5	0	1	0	0	0	1
5	1	2-4	1	1	2	2	11	17
Total			2	2	14	3	13	34

*See text.

Results of the classification of the 34 cases of Dp+ and Gp+ into the above five categories are presented in Table 2. Type 5 was the most common among these variants and found in 17 cases, consisting of 11 with 22p+, 2 each with 15p+ and 21p+, and one each with 13p+ and 14p+. Type 2 included eight cases all of which were 15p+. Five cases were classified as Type 1 and three cases as Type 3; the former consisting

34例のDp＋とGp＋を上述の五つのタイプに分類した結果を表2に示す．これらの変異体の中で最も多いのがタイプ5で，22p＋が11例，15p＋と21p＋がそれぞれ2例ずつ，13p＋と14p＋がそれぞれ1例ずつ，合計17例にみつかっている．タイプ2は8例で，すべて15p＋であった．タイプ1は5例，タイプ3

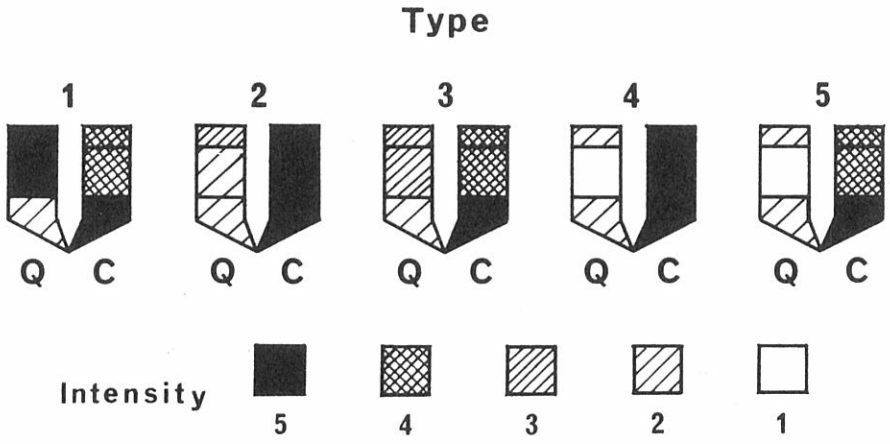

Figure 4. Diagramatic representation of the staining intensity of the proximal, middle, and distal regions of the enlarged short arm of Dp+ and Gp+, showing the Q-staining intensity in left chromatid and the C-staining intensity in right chromatid.

図4．Dp＋とGp＋の大きな短腕の基部，中間部，端部の染色性の模式図．左側の染色分体にはQ-法，右側の染色分体にはC-法の染色性が示してある．

of three with 15p+ and two with 22p+, and the latter having one each with 13p+, 15p+ and 21p+. One case with 14p+ was classified as Type 4.

Inasmuch as the above classification depends only on the staining intensity of the middle region of the enlarged short arm, the banding patterns of the proximal or distal regions varied among cases even for those classified as the same "Type", emphasizing the observation that the banding patterns of the entire short arm of Dp+ and Gp+ are, in fact, quite variable from case to case.

DISCUSSION

Enlargement of the short arms of D or G chromosomes has been demonstrated in a large number of individuals, mostly without phenotypic abnormalities.[12] However, identification of the variant chromosome using recently developed banding techniques has been described in only a few cases.[13–16] In the present study, it was found that 15p+ was the most common variant in Dp+ (14 cases out of 18) and the majority of the Gp+ was 22p+ (13 out of 16).

は3例あった．前者は3例の15p＋と2例の22p＋で，後者は13p＋，15p＋，21p＋それぞれ1例ずつであった．タイプ4には1例の14p＋が分類された．

上記の分類は大きい短腕の中間部のみの染色性によるものであり，基部や端部の分染パターンは同じ"タイプ"に分類されたものでも異なることがあり，これはDp＋とGp＋の短腕全体の分染パターンには著しい多様性があることを示している．

考察

DおよびG染色体の大きな短腕は多くの人々に認められており，それらのほとんどは表現型に異常は認められていない．[12]しかしながら，近年開発された分染法を用いて変異染色体を識別したのは数例にすぎない．[13–16]本調査によってDp＋の中で最も多い変異体は15p＋であり（18例中14例），Gp＋の大多数は22p＋である（16例中13例）ことが判明した．

The present observation on the enlarged short arm of Dp+ and Gp+ by the Q- and C-methods showed remarkable variation in their banding patterns among different cases, even though they belonged to the same chromosome pair. However, the proximal region of the enlarged short arms in all cases studied was stained very darkly by the C-method, and showed pale fluorescence by the Q-method, except for one case with 13p+ having a brilliant proximal region. On the other hand, very variable staining intensity was demonstrated in the middle and distal region; fluorescing brilliantly to negatively by the Q-method and very dark to light staining by the C-method. The region that fluoresced brilliantly was always stained rather darkly by the C-method, whereas the region stained very darkly by the C-method usually showed intermediate or pale fluorescence by the Q-method, except for one case. In this exceptional case, the middle region which was stained very darkly by the C-method fluoresced negatively by the Q-method.

Several cases of brilliantly fluorescing enlarged short arms of Nos.15 and 22 have been reported,[17-21] and it is assumed in these cases that the variant chromosomes are derived from a translocation between the long arm of the Y and the short arm of a No.15 or a No.22 chromosome. One of 15p+ cases studied here was suspected to have the enlarged short arm with the same banding pattern to that of the Yq. However, detailed analysis of the variant chromosome indicated that its C-staining intensity was slightly lighter than that of the Yq. So far in the cases examined by us none has been observed to exhibit the banding pattern of the enlarged short arm identical to that of the distal region of the Yq. This finding indicates that the cases with Dp+ and Gp+ studied here had not arisen from a translocation between the long arm of the Y and the short arm of the D or G chromosomes.

Jacobs et al[14] reported the banding patterns of the long short arm of a 15p+ and a 22p+ chromosome. The entire length of the short arm of the 15p+ was stained intensely by the C-method, but negatively using the Q- and G-methods, whereas the long short arm of the 22p+ had a bright fluorescent band and a rather dark staining band by both the C- and G-methods. The former variant presumably corresponds to the Type 2 15p+ and the latter to the Type 1 22p+ in the present study. A similar banding pattern to our Type 2 15p+ was also reported for a familial 15p+

Q-とC-法を用いてDp＋とGp＋の大きい短腕を分析したところ，その分染パターンはそれぞれの個体によって著しく異なっており，同一の染色体対に属するものでも違いがみられた．しかしながら，大きい短腕の基部は調べた全例においてC-法で非常に濃く染まり，Q-法で淡く光った．ただし例外として基部が強く光る13p＋が1例あった．一方，中間部と端部では染色性に著しい変異が認められた；Q-法で強く光るものから全く光らないものまであり，C-法で非常に濃く染まるものから薄く染まるものまであった．強く光る部位はC-法で常に幾分濃く染まり，他方C-法で非常に濃く染まる部位は通常Q-法で中程度あるいは淡く光った．ただし例外としてC-法で非常に濃く染まる中間部がQ-法で全く光らないものが1例あった．

強く光る大きな短腕をもつNo. 15やNo. 22染色体について数例の報告があり，[17-21]これらの変異染色体はNo. 15あるいはNo. 22の短腕とY染色体の長腕との間の転座によって形成されたと考えられている．本調査においても15p＋1例の大きい短腕がYqと同じ分染パターンを示しているようにみられたか，変異染色体を詳細に分析してみるとC-法による染色性がYqよりも少し薄いことがわかった．これまでのところ，Yqの端部と同じような分染パターンを示す大きな短腕はみつかっていない．このことは本調査におけるDp＋とGp＋の中にはYの長腕とDあるいはG染色体の短腕との間の転座に由来するものは含まれていないことを示している．

Jacobsら[14]は15p＋1例と22p＋1例の長い短腕の分染パターンを報告している．15p＋の短腕全体はC-法で強く染まるが，Q-とG-法では染まらない．一方，22p＋の長い短腕は強く光るがC-とG-法で共に幾分濃く染まる．前者は恐らく本報告におけるタイプ2の15p＋に相当し，後者はタイプ1の22p＋に相当すると思われる．大きな一家系にみられた遺伝的な15p＋変異体においてもタイプ2の15p＋と同じよう

variant in a large kindred.[15] The lightly stained p+ region with fluorescing satellites at the terminal end was entirely darkly stained by the C-method.

Tuncbilek et al[16] reported a giant short arm of No.21 chromosome in the mother of a Down's syndrome child with 21/21 translocation, showing positive staining intensity by the C-method and dull fluorescence by the Q-method. The banding pattern of the giant short arm of this 21p+ is almost identical to the Type 2 15p+ in the present study. However, three cases with 21p+ studied here did not show such banding patterns in the enlarged short arm.

The enlarged short arm in the Type 4 case described here was characterized by negative fluorescence by the Q-method and very dark staining intensity by the C-method. Such banding patterns are also observed in the secondary constriction of Nos. 1, 9 and 16 chromosomes. Moreover, by the G-staining method, the secondary constriction of Nos.1 and 16 are intensely dark whereas the heterochromatin of No. 9 is lightly stained; whether the heterochromatin of the enlarged short arm of the Type 4 case is similar to that of Nos. 1 and 16, or, alteratively, to No. 9, is not known, since G-banding analysis of our Type 4 case has not yet been done.

The enlarged short arm in Type 1 was characterized by brilliant fluorescence by the Q-method, and such brilliant fluorescence was frequently observed in the short arms of No.13 chromosome, the length of their short arm being within the normal range. However, Type 1 was found to include three cases with 15p+, two with 22p+ and none of 13p+, suggesting the possibility that these 15p+ and 22p+ may be derived from a translocation between the short arms of the variant chromosomes and the brilliantly fluorescing short arm of the No.13 chromosomes. Several cases of deletion of the short arm of the D chromosome (Dp−) were found in our sample, and all of them involved a No.13 chromosome (Sofuni et al, unpublished). This finding also suggests that these 13p− may be causally related to the brilliant fluorescing enlarged short arm of the Dp+ and Gp+.

The short arms of No.15 chromosomes were commonly stained darkly by the C-method and less frequently fluoresced brilliantly or intensely by the Q-method. Type 2 included only 15p+ and showed similar banding patterns to those of

な分染パターンが報告されている.[15] p+部位は淡く光り，端部の付随体は明るく光り，これらが全てC-法で濃く染まった.

Tuncbilek ら[16]は21／21転座のダウン症の子供の母親に大きな短腕をもつNo. 21染色体を報告しており，この短腕はC-法で濃染し，Q-法で淡く光った．この21p+の大きな短腕の分染パターンは本報告におけるタイプ2の15p+にほぼ一致している．しかしながら，本調査における3例の21p+の大きな短腕にはこのような分染パターンはみられなかった.

本報告におけるタイプ4の大きい短腕はQ-法で染まらず，C-法で非常に濃く染まるという特徴がある．このような分染パターンはNo. 1， 9， 16染色体の二次狭窄にもみられる．さらにG-染色法によってNo. 1と16の二次狭窄は濃く染まるが，No. 9の異質染色質は薄く染まる；タイプ4の短腕の異質染色質がNo. 1と16に似ているのか，あるいはNo. 9に似ているのかは，タイプ4についてG-法を用いて分析していないので明らかでない.

タイプ1の大きい短腕はQ-法で強く光るという特徴があるが，このような強い蛍光性はNo. 13染色体の短腕，しかもその長さが正常範囲内にあるものにおいてしばしば認められている．しかしながら，タイプ1には3例の15p+と2例の22p+とがあるが，13p+は1例も含まれていない．このことからこれら15p+と22p+がNo. 13染色体の強く光る短腕とNo. 15あるいはNo. 22染色体の短腕との間の転座によって生じた可能性が考えられる．本調査集団においてD染色体の短腕の欠失（Dp−）が数例みつかっており，これらが全てNo. 13染色体に関与していた（祖父尼ら，未発表）.このことはこれら13p−がDp+やGp+にみられる強く光る大きな短腕の成因と関連のあることを示唆している.

No. 15染色体の短腕は通常C-法で濃く染まるが，Q-法では強く光ったり明るく光ったりすることはまれである．タイプ2は15p+だけが含まれており，しか

the short arm of normal No.15 chromosomes. Therefore, it is conceivable that these Type 2 15p+ may be derived from duplication of the short arm of the No.15 chromosomes.

Type 3 is characterized by intermediate staining intensity by both Q- and C-methods. This banding pattern resembles that of the euchromatic rather than heterochromatic region. However, none of our data suggested that the enlarged short arm of Type 3 variant chromosomes may be caused by translocation or insertion of the euchromatic segment of certain chromosome.

In the Type 5, which comprised more Dp+ and Gp+ than any of the other types, the enlarged short arm was negatively stained by the Q-method and slightly darkly to lightly by the C-method. Since the short arm of the D and G chromosomes did not show negative fluorescence, the enlarged short arm of this type of Dp+ and Gp+ chromosomes may not be derived from a simple duplication of the short arm alone, but from the duplication of the short arm area including the nucleolus organizer region and satellite region. If the middle region fluoresced negatively by the Q-method is the nucleolus organizer region, it is still unclear why this region was stained positively by the conventional staining method, since this region in the normal D and G chromosomes was stained negatively by the conventional method.

The origin of the enlargement of the short arms of D or G chromosomes has been explained by several hypotheses, such as, alteration of coiling and condensation, pericentric inversion, duplication of the short arm and insertion or translocation.[22,23] The variability of the banding patterns of the enlarged short arms of the Dp+ and Gp+ demonstrated here suggests that the origin of the enlarged short arms of the Dp+ and Gp+ may be caused through two or more different mechanisms rather than in only one simple way.

At present, it is not clear whether the enlarged short arms of the Dp+ and Gp+ chromosomes studied here have the satellite region or not, since the morphological appearance of the enlarged short arm superficially resembles the usual short arm which has neither satellites nor

も正常のNo. 15染色体の短腕の分染パターンに似ている．それ故，これらタイプ2の15p＋はNo. 15染色体の短腕の重複によって生じた可能性が考えられる．

タイプ3の特徴はQ-とC-法の染色性がともに中程度という点にある．この分染パターンは異質染色質部位よりはむしろ真正染色質部位の分染パターンに似ている．しかしながら，タイプ3の変異染色体の大きな短腕が他の染色体の真正染色質からの転座あるいは挿入によって生じたことを示唆するような資料は何も得られていない．

タイプ5はDp＋とGp＋の中で他のどれよりも多くみられたもので，その大きな短腕はQ-法で染まらないが，C-法では濃く染まるものから薄く染まるものまである．DとG染色体の短腕にはQ-法で染まらない部位はないので，このタイプのDp＋とGp＋の大きい短腕は短腕だけの単純な重複によって生じたものではなく，仁形成部位や付随体を含む短腕部全体の重複によって生じたものと考えられる．もしQ-法で染まらない短腕中間部が仁形成部位であるとしても，正常のDとG染色体では仁形成部位は通常の染色法で染色されないのに，なぜ変異染色体の仁形成部位は通常の染色法で染まるのかはまだ明らかでない．

DあるいはG染色体の短腕の増大の成因についてはいくつかの仮説が考えられている．すなわち，染色体のらせん形成や凝縮の変化，挟動原体逆位，短腕の重複，挿入あるいは転座などである．[22,23] 本調査においてDp＋とGp＋染色体の大きな短腕の分染パターンに多様性が認められたことは，これらの大きな短腕の成因がたった一つの単純な機構によって生じたと考えるよりもむしろ二つあるいはそれ以上の異なった機構によって生じたと考える方が妥当であると思われる．

本調査におけるDp＋とGp＋染色体の大きな短腕に付随体が含まれているか否かについては現時点においてはわからないが，通常の染色法による大きな短腕の形態は表面的には正常の短腕に似ており，付随

distinct stalks when stained by the conventional method. However, it is possible that several cases of Dp+ and Gp+, especially those classified as Type 5, in which the middle region fluoresced negatively by the Q-method, may have the satellites and the nucleolus organizer region. Recently developed new techniques which specifically stain the nucleolus organizer region[24,25] may yield information concerning the nucleolus organizer region and satellites in the enlarged short arm of Dp+ and Gp+, and also provide an opportunity to study and understand the underlying cause of the enlarged short arm of these variant chromosomes.

体や明瞭な二次狭窄は認められていない．しかし，これらDp＋とGp＋のあるもの，特にタイプ5に分類されたものは短腕の中間部がQ-法で染まらないことから，付随体や仁形成部位を含んでいる可能性が考えられる．最近，仁形成部位を特異的に染める方法が新たに開発されており，[24,25]これによってDp＋とGp＋の大きな短腕における仁形成部位と付随体について調べることができるとともに，これら変異染色体の大きな短腕の成因について検討を加えることも可能である．

REFERENCES
参考文献

1. CRAIG-HOLMES AP, MOORE FB, SHAW MW: Polymorphism of human C-band heterochromatin. I. Frequency of variants. Am J Hum Genet 25:181-92, 1973

2. MCKENZIE WH, LUBS HA: Human Q and C chromosomal variations: distribution and incidence. Cytogenet Cell Genet 14:97-115, 1975

3. MÜLLER H, KLINGER HP, GLASSER M: Chromosome polymorphism in a human newborn population. II. Potentials of polymorphic chromosome variants for characterizing the idiogram of an individual. Cytogenet Cell Genet 15:239-55, 1975

4. BUCKTON KE, O'RIORDAN ML, JACOBS PA, ROBINSON JA, HILL R, EVANS HJ: C- and Q-band polymorphisms in the chromosomes of three human populations. Ann Hum Genet 40:99-112, 1976

5. JACOBS PA: Human chromosome heteromorphisms (variants). In *Progress in Medical Genetics – New Series,* ed by Steinberg AG, Bearn AG, Motulsky AG, Childs B. Philadelphia, London, Tront, Saunders Co., 1977. Vol. II, pp. 251-74

6. KATO H, SCHULL WJ, NEEL JV: A cohort-type study of survival in the children of parents exposed to atomic bombings. Am J Hum Genet 18:339-73, 1966

7. BEEBE GW, USAGAWA M: The Major ABCC samples. ABCC TR 12-68

8. CASPERSSON T, LOMAKKA G, ZECH L: The 24 fluorescence patterns of the human metaphase chromosomes – distinguishing characters and variability. Hereditas 67:89-102, 1971

9. SUMNER AT: A simple technique for demonstrating centromeric heterochromatin. Exp Cell Res 75:304-6, 1972

10. Paris Conference (1971) Supplement (1975): Standardization in human cytogenetics. Birth Defects, Original Articles Series XI; 9. New York, The National Foundation, 1975

11. Paris Conference (1971): Standardization in human cytogenetics. Cytogenetics 11:313-62, 1972

12. SOUDEK D: Chromosomal variants with normal phenotype in man. J Hum Evol 2:341-55, 1973

13. MIKELSAAR AVN, TÜÜR SJ, KÄOSAAR ME: Human karyotype polymorphism. I. Routine and fluorescence microscopic investigation of chromosomes in a normal adult population. Humangenetik 20:89-101, 1973

14. JACOBS PA, MELVILLE M, RATCLIFFE S, KEAY AJ, SYME J: A cytogenetic survey of 11,680 newborn infants. Ann Hum Genet 37:359-76, 1974

15. YODER FE, BIAS WB, BORGAONKAR DS, BAHR GF, YODER II, YODER OC, GOLOMB HM: Cytogenetic and linkage studies of a familial 15p+ variant. Am J Hum Genet 26:535-48, 1974

16. TUNCBILEK E, BOBROW M, CLARKE G, TAYSI K: A giant short arm of no. 21 chromosome in mother of 21/21 translocation mongol. J Med Genet 13:411-2, 1976

17. NOEL B, EMERIT I, LUCIANI JM, QUACH B: A familial Y/autosome translocation in man. Clin Genet 2:1-6, 1971

18. FRÜND S, KOSKE-WESTPHAL T, FUCHS-MECKE S, PASSARGE E: Quinacrine mustard fluorescence of a second Y chromosome in a Y-autosomal translocation. Humangenetik 14:133-36, 1972

19. FRIEDRICH U, NIELSEN J: Presumptive Y-15 and Y-22 translocation in two families. Hereditas 71:339-42, 1972

20. PFEIFFER RA, BIER L, MAJEWSKI F, RAGER K: *De novo* translocation t(Yq−; 15p+) in a malformed boy. Humangenetik 19:349-52, 1973

21. NIELSEN J, RASMUSSEN K: Y/autosomal translocations. Clin Genet 9:609-17, 1976

22. SANDS VE: Short arm enlargement in acrocentric chromosomes. Am J Hum Genet 21:293-304, 1969

23. HOSSFELD DK, IKEUCHI T, SANDBERG AA: Chronology and pattern of human chromosome replication X. Autoradiographic studies of an abnormal familial chromosome of the D(13-15) group. Cytogenetics 9:351-9, 1970

24. MATSUI S, SASAKI M: Differential staining of nucleolus organizers in mammalian chromosomes. Nature 246:148-50, 1973

25. BLOOM SE, GOODPASTURE C: An improved technique for selective silver staining of nucleolar organizer regions in human chromosomes. Hum Genet 34:199-206, 1976