ECG) was monitored continuously. The jugular vein was cannulated on one side for intravenous (i.v.) drug administration. Rats were placed in a Kopf stereotaxic device (with the top of the skull level), and a bipolar stainless-steel microelectrode insulated to 0.5 mm of the tip was inserted to a depth of 0.5 to 1.2 mm from the cortical surface to record electroencephalographic (EEG) activity in the fronto-parietal cortex. Data were stored on VHS videotape and analyzed off-line. After the surgical preparation and electrode placement, animals were allowed to recover for 30 min before the experiments were initiated with an injection of kainic acid (10 to 12 mg/kg, i.v.). Intense electrographic seizure activity, an increased heart rate, and rapid movements of the vibrissae were induced with a latency of about 30 min. Strong nociceptive stimulation of the hind paw was performed intermittently to ensure that no response was produced, indicating that a sufficient level of anesthesia was maintained [S. C. Baraban, R. L. Stornetta, P. G. Guynet, *Brain Res.* **676**, 245 (1995); R. S. Sloviter, *Hippocampus* **1**, 31 (1991)]. Once stable electrical seizure activity was evident, furosemide was delivered in 20 mg/kg boluses every 30 min up to a total of three injections. Experiments were terminated with the i.v. administration of urethane. Animal care was in accordance with NIH guidelines and approved by the University of Washington Animal Care Committee.

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Discrete Cortical Regions Associated with Knowledge of Color and Knowledge of Action

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The areas of the brain that mediate knowledge about objects were investigated by measuring changes in regional cerebral blood flow (rCBF) using positron emission tomography (PET). Subjects generated words denoting colors and actions associated with static, achromatic line drawings of objects in one experiment, and with the written names of objects in a second experiment. In both studies, generation of color words selectively activated a region in the ventral temporal lobe just anterior to the area involved in the perception of color, whereas generation of action words activated a region in the middle temporal gyrus just anterior to the area involved in the perception of motion. These data suggest that object knowledge is organized as a distributed system in which the attributes of an object are stored close to the regions of the cortex that mediate perception of those attributes.

During our lifetimes we acquire knowledge about a tremendous number of concrete objects. This knowledge includes not just the name, but also the physical features (form and color) and functional properties (uses) that define each object. When an object is seen or its name read, knowledge of these attributes is activated automatically and without conscious awareness (*1*). In addition, the ability to retrieve information about a specific attribute of an object can be selectively disrupted by a focal brain lesion (*2*, *3*). These findings suggest that object knowledge is stored in the brain as a distributed network of discrete cortical areas (*4*). However, direct evidence for the existence of such a network in the normal human brain has not been reported, nor have the component areas of the network been identified. We show, using positron emission tomography (PET), that the attributes that define an object are represented close to the cortical regions that mediate perception of those attributes.

We chose to study knowledge of color and action because evidence from monkeys (*5*) and humans (*6*–*8*) suggests that the perception of these attributes is mediated, in part, by discrete regions of the posterior cortex. In humans the syndrome of acquired color blindness, or achromatopsia, has been found after damage to the fusiform and lingual gyri on the ventral surface of the occipital lobes (*6*, *7*), whereas acquired motion blindness, or akinetopsia, follows a more dorsally located lesion at the junction of the occipital, parietal, and temporal lobes (*7*, *8*). Converging evidence that these regions are specialized for the perception of color and motion, respectively, has been provided by functional brain imaging studies of normal individuals (*9*, *10*). Moreover, reports of patients with selective difficulty retrieving information about object-associated color (*2*) or action (*3*), without corresponding deficits in perception, suggest that knowledge of these attributes also may be mediated by distinct brain areas (*11*).

In the first study (*12*), achromatic line drawings of common objects were present-

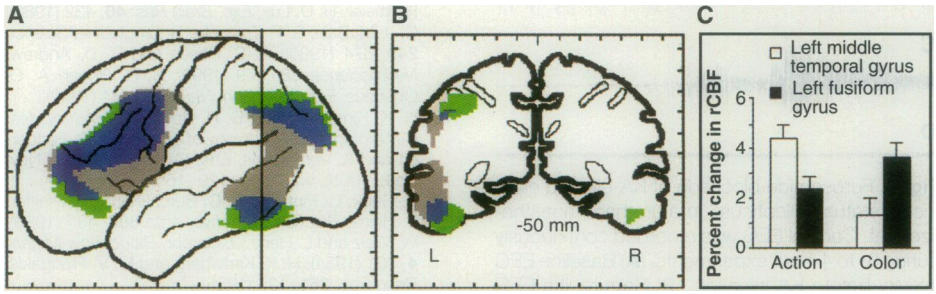

Fig. 1. (**A**) Lateral view of the left hemisphere showing regions of increased rCBF when subjects generated color words (green) and action words (gray) in comparison to object naming. Dark blue regions show areas of overlap. (**B**) Coronal section 50 mm posterior to the anterior commissure showing locations of bilateral fusiform and left parietal lobe activation during color word generation, and left temporal and parietal activations during action word generation. Shown are all pixels that exceeded a threshold of $Z = 2.58$ ($P < 0.005$, one-tailed). (**C**) Percent change in rCBF, relative to object naming, at the site of peak activity in the left middle temporal gyrus (open bar) (−50, −50, 0) and left fusiform gyrus (closed bar) (−46, −46, −12) shown in (B). Bars represent mean percent change in rCBF ± SEM. Analysis of variance indicated that rCBF at these sites was modulated by the type of word that subjects generated [site X task interaction $F(1,11) = 21.66$; $P < 0.001$].

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ed. During separate PET scans, subjects were required to name each object, to generate the name of a color associated with each object (for example, a subject might say "yellow" when shown a picture of a pencil), and to generate the name of an action associated with each object (for example, "write" when shown a picture of a pencil) (*13*). Verbal response times recorded during the scans confirmed that the color and action word generation tasks were equally difficult (*14*), thus assuring that differences in the brain regions activated by generating color and action words would not reflect differences in the amount of effort required to perform these tasks.

Our strategy for analyzing the rCBF data (*15*) was first to compare each attribute word generation task to the same baseline condition (object naming). These comparisons revealed areas of activation common to both attribute word generation tasks as well as the areas specifically activated by each task, over and above the amount of activation produced by object naming. The areas specifically activated by each attribute word generation task were confirmed by a second analysis in which the color and action word tasks were directly contrasted with each other.

In comparison to object naming, generation of color and action words activated left prefrontal cortex, especially the dorsolateral region, and left posterior parietal cortex (Fig. 1 and Table 1). These regions participate in distributed neural networks (*16*) that mediate specific language processes, especially word retrieval (*17*), and attentional functions (*18*) and that would be expected to be engaged by both attribute generation tasks.

In contrast, activation of other areas was dependent on the type of word generated. Within the temporal lobes, generation of color words, but not action words, produced bilateral activation ventrally on the fusiform gyrus that was stronger in the left than in the right hemisphere, whereas generation of action words activated the left posterior middle and superior temporal gyri. Action word generation also produced increased rCBF in the left inferior frontal lobe (Broca's area) and in the right lateral cerebellum (Table 1). These word-specific patterns of activation were confirmed by comparison of the color and action word generation conditions to each other (Fig. 2).

To replicate and extend these findings, we performed a second study that was identical to the first, except that the written names of the objects, rather than line drawings, were presented. During different scans subjects read aloud, generated a color word, and generated an action word associated with the written name of each object. As in the first study, generating words denoting either colors or actions was equally difficult (*19*). Despite the change in stimulus from line drawings of objects to their written names, the areas of increased activation specifically associated with the word generation tasks were highly similar to the activations found in the first study. Relative to the action word generation condition, increased rCBF during color word generation was seen in the ventral portion of the right temporal lobe (Fig. 2A). In contrast, relative to the color word generation condition,

Table 1. Brain regions with significantly increased rCBF during generation of color and action words compared to object naming. Numbers in parentheses refer to the corresponding Brodmann's areas. Locations of peak activations are expressed in millimeters as coordinates in the Talairach and Tournoux brain atlas (*28*). *x*, medial-lateral axis (negative, left); *y*, anterior-posterior axis (negative, posterior); and *z*, dorsal-ventral axis (negative, ventral).

Brain region	*x*	*y*	*z*	*Z* score
Color word generation minus object naming				
Frontal lobe				
Left middle frontal gyrus (8/9)	−42	18	28	5.35
Left middle frontal gyrus (45/46)	−38	30	20	4.90
Left orbital frontal gyrus (11)	−24	32	−8	3.48
Parietal lobe				
Left inferior parietal gyrus (40)	−34	−62	40	4.59
Temporal lobe				
Left fusiform gyrus (37)	−46	−46	−12	5.20
Left parahippocampal gyrus (35)	−18	−42	4	2.99
Right fusiform gyrus (37)	44	−48	−12	2.97
Thalamus				
Right pulvinar	6	−28	8	3.64
Action word generation minus object naming				
Frontal lobe				
Left inferior frontal gyrus (44/45)	−42	12	20	4.87
Left middle frontal gyrus (6)	−36	4	44	4.71
Left Broca's area (44)	−43	18	6	3.98
Left middle frontal gyrus (9/10)	−34	48	16	3.67
Left inferior frontal gyrus (45/47)	−32	34	0	3.30
Parietal lobe				
Left inferior parietal gyrus (40)	−38	−64	36	3.49
Temporal lobe				
Left middle temporal gyrus (21/37)	−52	−50	0	4.77
Left middle temporal gyrus (37)	−46	−60	16	3.47
Left superior temporal gyrus (39)	−50	−62	28	3.57
Cerebellum				
Right lateral cerebellum	26	−68	−28	4.48

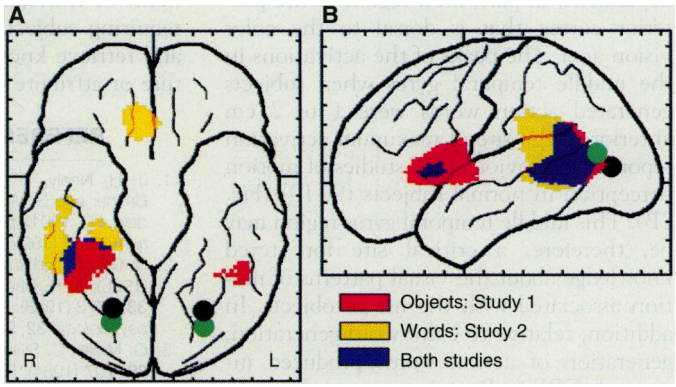

Fig. 2. (**A**) Ventral view of the brain showing regions of increased rCBF when subjects generated color words in comparison to generating action words. (**B**) Lateral view of the left cerebral hemisphere showing regions of increased rCBF when subjects generated action words in comparison to generating color words. Red indicates activations in response to line drawings of objects; yellow indicates activations in response to the written names of the objects; and blue indicates regions activated in both studies. Also shown are black (*9*) and green (*10*) circles centered on previously reported locations of maximum activity during the perception of color (A) and of motion (B). Maximum peaks of activity during color word generation (A) were in the fusiform gyri of the left (−42, −46, −12) and right (+42, −42, −20) temporal lobes for the object study, and the fusiform (+50, −38, −12) and parahippocampal gyri (+28, −30, −16) of the right temporal lobe, and orbital frontal cortex (+12, +26, −12) for the word study (*29*). For action word generation (B) peak activations were in the left inferior frontal lobe (Broca's area) (−44, +6, +4; and −42, +18, +4), and in the middle (−50, −50, +4; and −54, −62, +8) and superior (−50, −52, +24; and −54, −38, +20) left temporal gyri during the object and word studies, respectively (*30*). Shown are all pixels that exceeded a threshold of $Z = 2.58$ ($P < 0.005$, one-tailed).

generation of action words produced increased activity of the same regions of the left temporal lobe (posterior middle and superior temporal gyri) and left inferior frontal lobe (Broca's area) found for generating action words to drawings of objects (Fig. 2B).

These results provide strong evidence that knowledge of colors and of actions is represented in discrete cortical areas (*20*). A distinctive feature of both studies is that responses to stimuli that were achromatic and static were nevertheless associated with activations proximal to color and motion perceptual-processing areas.

Studies of nonhuman primates (*21*) and PET studies of humans (*22*) have shown that object vision is mediated by a hierarchically organized ventral occipitotemporal pathway that includes distinct regions for processing visual features of objects, such as form and color. In the present study the areas of the temporal lobe specifically activated by retrieving knowledge about object color were in this object-processing stream. The peaks of these activations were 2 to 3 cm anterior to the site of maximum activity in the fusiform gyrus reported in previous PET studies of color perception in normal subjects (*9*, *10*) (Fig. 2A). That the action and color word generation conditions required perception and identification of the same objects suggests that the activation in the fusiform region in the present study reflects its role in the representation of knowledge of object color, rather than of object form. Thus, damage to this area may be necessary for producing color anomia or color agnosia (*2*).

Studies of nonhuman primates (*21*) and PET studies of humans (*9*, *10*) have also shown that the perception of motion is dependent, in part, on a region of the posterior cortex that is dorsal to the color vision area. The peaks of the activations in the middle temporal gyrus when subjects generated action words were 1 to 2 cm anterior to the site of maximum activation reported in previous PET studies of motion perception in normal subjects (*9*, *10*) (Fig. 2B). This middle temporal gyrus region may be, therefore, a critical site for stored knowledge about the visual patterns of motion associated with the use of objects. In addition, relative to color word generation, generation of action words produced increased rCBF in Broca's area and the right cerebellum, as reported previously in PET studies of verb generation to presentation of printed words (*23*). Damage to Broca's area often produces a general disruption of speech characterized by a severe restriction of small function words, such as prepositions, and an impoverishment of grammatical forms, suggesting that this region plays an important role in speech production and grammar (*24*). Production and comprehension of verbs relative to nouns are often disproportionally affected in these patients (*3*). Our data indicate that generation of action verbs increases activity in this region over and above the level produced by simple naming, whereas color word generation does not. This additional activation of Broca's area may be related to the special role that verbs play in grammatical sentence constructions. Action word generation appears to activate a complex neural network that may be related to both the semantic aspects associated with knowledge of motion (middle temporal gyrus) and grammatical functions of verbs (Broca's area).

Whereas PET studies of visual perception have shown that activity in different regions of the brain can be modulated by attention to different visual features of an object (*10*), the present results indicate that activity in different regions can be modulated by attention to knowledge about different features (*25*). Our findings suggest that object knowledge is stored as a distributed network of cortical regions and that the organization of these regions may closely parallel the organization of sensory, and perhaps also motor, systems in the human brain (*26*). We further suggest that the perception of objects and their written names automatically activates a widely distributed network that includes the areas active during color and action word generation, as well as sites that mediate knowledge of other object attributes. Activation of this network occurs without conscious effort and lasts for only a brief period of time (*1*). It remains to be determined whether this automatic activation can be detected by PET during object naming and word reading. However, different components of this network can be observed by requiring subjects to selectively attend to and retrieve knowledge about a single feature or attribute of an object.

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11. These clinical cases are rare and commonly have large lesions. As a result, the cortical regions that mediate knowledge of these and other object attributes have not been identified.
12. Twelve (nine male and three female) strongly right-handed subjects {Edinburgh Handedness Inventory [R. C. Oldfield, *Neuropsychologia* **9**, 97 (1971)]} participated in the study (age range, 22 to 40 years; mean, 27.6 years). Informed consent was obtained in writing.
13. Stimuli depicted manufactured objects [most from J. G. Snodgrass and M. Vanderwart, *J. Exp. Psychol. Hum. Learn. Mem.* **6**, 174 (1980)] and were presented in the center of a video monitor for 180 ms, followed by a centrally located fixation cross for 1820 ms. Subjects were instructed to limit their response to a single word and were familiarized with the tasks ~24 hours before scanning with practice items. During each scan 50 items were presented. A fixed set of 35 items occurred in random order at the beginning and end of the list (the first 13 and last 22 objects). These items served as a buffer to engage subjects in the desired mode of processing and to provide data on consistency of responses to the same objects across subjects. The intervening 15 items were seen by a subject only once during the experiment. These 15-item lists were equated for name frequency [H. Kucera and W. N. Francis, *Computational Analysis of Present-day American English* (Brown Univ. Press, Providence, RI, 1967)], categories, and category typicality ranking [W. F. Battig and W. E. Montague, *J. Exp. Psychol. Monogr.* **80** (no. 3), part 2 (1969)] and were counterbalanced across subjects and conditions. The start time of the task was adjusted to ensure that measurement of rCBF during the critical first 20 to 30 s of the 60-s scan coincided with the presentation of the 15-item lists [R. R. Hurtig *et al.*, *J. Cereb. Blood Flow Metab.* **14**, 423 (1994)].
14. Mean ± SEM for voice response time = 822 ± 29.7 ms for generating color words and 797 ± 28.9 ms for generating action words ($P > 0.10$). Errors, primarily failures to respond, were rare (<5% of the items), and error rates did not differ significantly for the color and action tasks. Agreement among subjects (the proportion of subjects retrieving the same word to the same object) did not differ significantly for the color and action tasks.
15. PET scans were obtained with a Scanditronix PC2048-15B tomograph (Milwaukee, WI) which acquires 15 contiguous, 6.5-mm-thick cross-sectional images. Within-plane resolution is 6.5 mm (full width at half maximum). Subjects began the task ~30 s before injection of 37.5 mCi of $H_2{}^{15}O$. Scanning began when the brain radioactivity count reached a threshold value and continued for 60 s. Head movement was minimized by a thermoplastic mask that was molded to each subject's head and attached to the scanner bed. Data were analyzed by statistical parametric mapping (SPM) [K. J. Friston *et al.*, *J. Cereb. Blood Flow Metab.* **9**, 690 (1989); K. J. Friston *et al.*, *ibid.* **10**, 458 (1990); K. J. Friston, C. D. Frith, P. F. Liddle, R. S. J. Frackowiack, *J. Comput. Assisted. Tomogr.* **15**, 634 (1991)]. Prior to SPM analysis, movement between scans was corrected with a program based on an algorithm described by Mintun [K. S. Lee, K. L. Berger, M. A. Mintun, *J. Cereb. Blood Flow Metab.* **11** (suppl. 2), S557 (1991)]. Data from each subject were normalized to his or her own global mean flow (ratio correction). Contrasts between tasks were evaluated by *t* tests and then converted to *z* scores.
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19. Twelve (nine male and three female) strongly right-handed subjects (age range, 23 to 36 years; mean, 27.6 years) who had not participated in the object study were tested. Informed consent was obtained in writing. The written names of the objects used in the first experiment were presented. Stimulus presentation parameters were identical to those used in the first experiment. Mean ± SEM for voice response time = 901 ± 29.2 ms for generating color words and 886 ± 26.6 ms for generating action words ($P > 0.10$).
20. Findings from studies of patients with focal brain lesions argue against alternative interpretations of these activations as the sites for storage of the color and action words themselves, or of word-specific retrieval mechanisms located at sites distant from those where information is stored. A patient with a color anomia can produce color words. What the patient cannot do is correctly name the colors seen or correctly answer questions about object-associated colors (the patient will respond with an inappropriate color word). To show areas of activity by functional brain imaging technologies, it is necessary for subjects to be engaged in performing a task. Thus, it might be formally more accurate to state that the activations in the temporal lobes show the sites of storage during the act of retrieval. In this sense, however, storage and retrieval cannot be distinguished.
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25. An important question that remains to be resolved concerns the role of mental imagery in eliciting the activations associated with the attribute word generation tasks. Most subjects reported color and motion imagery while generating color words and action words, respectively. It has been proposed that mental imagery is dependent on the top-down influence of brain areas that contain stored representations on lower-level visual-processing areas in the occipital lobe (*27*). Evidence that the occipital cortex may serve as the representational medium for visual images has been obtained from studies of patients with focal lesions [M. J. Farah, M. J. Soso, R. M. Dasheiff, *J. Exp. Psychol. Hum. Percept. Perform.* **18**, 241 (1992)] and from PET studies of normal individuals (*27*). Our failure to observe activity in the occipital cortex during the word generation tasks could have resulted from the involvement of mental imagery or lower-level visual processing (or both) in the baseline tasks. The regions identified in our study might also be activated, perhaps in concert with the occipital cortex, if subjects were explicitly instructed to imagine objects in a particular color and to imagine objects being used. If so, our findings would suggest that different components of an image, such as color and motion, would depend on the activation of representations of object color stored in the ventral temporal lobe and representations of object action stored in the middle temporal gyrus.
26. Neither frontal nor parietal regions involved in object manipulation and visual guidance of reaching and grasping were selectively activated when subjects produced action words. Failure to activate these regions may reflect the fact that many of the objects used in the studies would not normally be experienced by reaching, grasping, or manipulation. Examples (followed by the most common response) include wheel (roll), cannon (shoot), helicopter (fly), telescope (see), gate (open), bed (sleep), and chair (sit). Objects were not limited to small, manipulable items such as tools because these items invariably elicit "silver" or "gray" as color responses. Brain regions close to those that are active during the actual manipulation of objects may be activated if subjects generated action words only in response to small, manipulable objects.
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29. Additional regions of activity were located in the inferior frontal (+32, +22, +16), inferior parietal (+48, −46, +32), and parietal-occipital sulcus (+18, −70, +32) of the right hemisphere in the object study, and the left mid-frontal region (−24, +20, +40) in the word study.
30. Additional regions were located in the right cerebellum: (+18, −72, −28 and +4, −44, −24) in the object study and (+42, −76, −20) in the word study.
31. We thank R. Desimone and R. Parasuraman for comments on the manuscript.

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Dependence of Peptide Binding by MHC Class I Molecules on Their Interaction with TAP

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Major histocompatibility complex (MHC) class I molecules bind peptides that are delivered from the cytosol into the endoplasmic reticulum by the MHC-encoded transporter associated with antigen processing (TAP). Peptide capture by immature heterodimers of class I heavy chains and β_2-microglobulin may be facilitated by their physical association with TAP. A genetic defect in a human mutant cell line causes the complete failure of diverse class I heterodimers to associate with TAP. This deficiency impairs the ability of the class I heterodimers to efficiently capture peptides and results from loss of function of an unidentified gene or genes linked to the MHC.

MHC class I molecules export peptides derived from cytosolic protein degradation to the cell surface and thus enable cytotoxic T cells to detect intracellular antigen (*1*). They consist of a membrane-anchored polymorphic class I heavy chain, soluble β_2-microglobulin (β_2M), and a peptide ligand of 8 to 10 amino acids with an allele-specific sequence motif (*2*). The complete subunit assembly of class I molecules is usually required for their conformational stability, maturation, and normal surface expression and involves accessory molecules (*2*). Upon entering the endoplasmic reticulum (ER), newly synthesized human class I heavy chains are retained by calnexin until they combine with β_2M (*3*). The immature class I heavy chain–β_2M heterodimers then associate with TAP transporters (*4*), which consist of the MHC-encoded TAP1 and TAP2 subunits and deliver the peptides that are mainly bound by class I heterodimers from the cytosol into the lumen of the ER (*5–7*). This physical interaction may be coupled to peptide binding by class I heterodimers, because dissociation from TAP correlates with their conversion into stably conformed class I molecules. Thus, by interacting with TAP, class I heterodimers may gain access to peptides before these may be diluted and possibly degraded in the lumen of the ER. However, it is unknown whether this proposed mechanism promotes peptide binding by class I heterodimers in living cells.

In defining the assembly of class I molecules, mutant cell lines with specific defects have been instrumental. In the human mutant lymphoblastoid cell line (LCL) 721.220, an unknown defect impairs the surface expression of class I molecules. These cells express functional β_2M and TAP, as indicated by transcomplementation of Daudi (β_2M^-) and mutant LCL 721.174 (TAP^-) cells after fusion (*8*). These cells have been isolated after repeated mutagenesis and selection against the surface class I molecules encoded in a hemizygous MHC, resulting in deletion of *HLA-A* and *-B* and in reduced surface levels of HLA-C (*9*). However, as with HLA-C, 220 cells are also unable to express normal surface amounts of several HLA-A and -B alleles after gene transfer–mediated reconstitution of biosynthesis of various class I heavy chains (*8*).

To investigate this mutant phenotype, we transfected HLA-A1 and -B8 complementary DNA (cDNA) constructs into 220 and control C1R cells, which also lack functional *HLA-A* and *-B* genes but are

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