with a linear current–voltage relationship over the whole range of voltages tested (Fig. 4g). The voltage-independent currents were identified as NADPH-oxidase currents on the basis of the following criteria: first, as expected for a unidirectional electron transporter, the currents were inward over the entire voltage range tested (−100 mV to +60 mV); second, the currents were blocked by DPI; third, the currents were resistant to the H^+-current inhibitor Zn^{2+}; and fourth, the replacement of CsCl in the solutions with the impermeant ions *N*-methyl-D-glycine ($NMDG^+$) and $HEPES^-$ did not modify the currents (not shown).

A puzzling observation of our study is the low threshold of voltage activation of the H^+ conductance under experimental conditions that support NADPH-oxidase activity. This can be seen most clearly during a voltage step from 0 mV to −80 mV in control cells (Fig. 4d, e). The deactivating tail seen under these conditions shows that the H^+ conductance was activated at 0 mV. Theoretically, however, the H^+ conductance is expected to be activated at voltages of around +40 mV in the presence of a pH gradient of 0.5 pH units (ref. 20). DPI shifted the threshold of voltage activation of the H^+ conductance towards the more positive voltages expected for our experimental conditions, as shown by the disappearance of the deactivating tail (Fig. 4d, f). No tail currents at −80 mV (that is, the sign of activated H^+ conductance at 0 mV) were observed with other conditions that precluded NADPH-oxidase activation (for example, in CGD eosinophils or under conditions of no oxygen, Fig. 4f). Thus, there is a functional coupling between NADPH oxidase and the H^+ conductance. Further studies will be necessary to elucidate the mechanism of coupling.

Our study is the first to demonstrate electron currents across the plasma membrane of a eukaryotic cell. These currents are generated by the phagocyte NADPH oxidase. The precise functions of the NADPH oxidase in host defence remain to be defined, however. The direct product of the NADPH-oxidase reaction, superoxide, is a relatively unreactive oxygen metabolite and its importance in microbial killing is unclear[4]. Our results indicate that the NADPH oxidase can generate large currents, even against major electrical gradients (Fig. 4g). This feature is unique compared with other electrogenic processes and might be—by itself—a biologically relevant function of the NADPH oxidase. Electron transport is a biologically relevant function of enzymes in, for example, bacteria, mitochondria and chloroplasts, where it generates protonmotive forces necessary for crucial cellular processes such as ATP generation or transport of protonated molecules[1,21]. Perhaps electron currents are involved in analogous vectorial transport in the phagocyte. □

Methods

Patients. The G6PD patient was a 36-year-old white male with an erythrocyte glucose-6-phosphate dehydrogenase activity of 0.25 units per g haemoglobin (normal range: 3.5–5.5). CGD patient 1 was a 33-year-old white male with X-linked CGD. CGD patient 2 was a 33-year-old white female with $gp47^{phox}$-negative CGD. The carrier was a 35-year-old healthy white female, whose brother had X-linked CGD[22].

Purification. Purification of eosinophils and whole-cell patch-clamp studies[15], noise analysis[23], $[Ca^{2+}]_c$ measurements[24], NBT staining[13], and oxygen depletion[17] were performed as described.

Solutions. If not indicated otherwise, the following solutions were used: bath solution: 75 mM CsCl, 50 mM CsOH, 50 mM HEPES/pH 7.1, 10 mM tetraethyl ammonium chloride (TEACl), 1 mM $MgCl_2$, and 0.1% glucose; pipette solution: 75 mM CsCl, 50 mM CsOH, 50 mM HEPES/pH 7.6, 10 mM TEACl, 1 mM $MgCl_2$, 1 mM MgATP, and 8 mM NADPH.

Statistics. Data are expressed as mean ± s.e.m. For statistics, a Wilcoxon sign-rank test with a level of significance $\alpha = 0.05$ was used.

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correction

A late Neanderthal associated with Upper Palaeolithic artefacts

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One of the important morphometric variables assessed in the comparisons between the bony labyrinths of Neanderthals and modern humans is the sagittal labyrinthine index. This index expresses what percentage of the posterior semicircular canal is situated inferiorly to the plane of the lateral semicircular canal. Its formula, as given in the legend to Fig. 2 of the above Letter, is incorrect and should be $i/(s + i) \times 100$. □