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Comment on the multi-person interview: "The future of research universities"

As the interviewees in *EMBO reports*' recent multi-person interview on the future of research universities made clear, universities continue to play a crucial role in the future of knowledge-based economies at the beginning of the twenty-first century. Although universities have also played a vital role in the invention and success of industry-based capitalism in the preceding centuries (Nelson, 1990), the current political and economic changes towards a knowledge-based society might be the main determinants for the future of research universities. The knowledge-based society itself is the result of a change in market capitalism to 'technocapitalism', which is characterized by its reliance on scientific research and technological innovations (Suarez-Villa, 2000, 2001, 2003).

Intangible values, such as creativity and knowledge, are the commodities of technocapitalism, as much as tangible raw materials, labour and capital were the commodities that underpinned industrial capitalism (Suarez-Villa, 2000, 2001). In fact, the emergence of technocapitalism has made knowledge such a valuable commodity—accounting for 75% of the value of most of the existing products and services in the world today—that material commodities now occupy secondary positions (Suarez-Villa, 2000, 2001).

The interaction between technocapitalism and science is also generating new networks for collaboration and disciplines for technological innovation—for example, biotechnology, nanotechnology, informatics and genomics. Both public and private enterprises are driven by research and innovation, which is in sharp contrast to industrial capitalism's entrepreneurs who focus more on production (Suarez-Villa, 2000). Societies that are aspiring to raise their citizens' living standards in the new era of technocapitalism must therefore invest heavily in fostering creativity and generating knowledge (Suarez-Villa, 2000). In this regard, the role of institutions of higher learning is pivotal in educating the next generation of scientists and engineers.

However, it is important to analyse how the relationship between technocapitalism and academic institutions—the traditional homes of science and technology—is changing. During the past 50 years, universities and industry have forged closer ties—which might reflect the marked expansion in science and technology education, and the unprecedented increase in physical infrastructure such as educational facilities and research laboratories—which has given rise to the university–industrial complex (Kenney, 1998). Not surprisingly, there are growing concerns about the effects that the commercialization of university research would have on the university as an independent intellectual institution (Kenney, 1998; Press & Washburn, 2000; Oehmke, 2005).

Apart from threats to the intellectual independence of science and technology departments, there might also be deleterious effects on the humanities. The emergence of the university–industrial complex puts a price-tag on research departments based on how much industrial money they can attract, which leads to the downsizing of humanity faculties. Hunter Rawlings, former President of Cornell University (Ithaca, NY, USA), argued in a public address that the tendency to be driven by financial considerations can lead to short-sighted emphasis on research fields with commercial potential and the neglect of others (Rawlings, 2000). The humanities have been providing important insights into and serious critique of the influence of science on society; they have enlarged our worldview, and act as the keepers and conveyors of culture in a democratic society. Since Socrates, the humanities have been catalysts for social change, providing society with a critical spirit and arguments (Rawlings, 2000); their loss would come at great cost to global society and thus to universities themselves.

Despite the rise of technocapitalism's university–industrial complex, it could be argued that the university has outlived its traditional role as the guardian of national culture (Readings, 1998). The rise of technocapitalism is a compulsory response to the evolution of capitalism as the engine of progress in modern society (Nelson, 1990). Unless there is a reversal in the trend of declining public funding to academic institutions, the future of research universities will be intimately linked to changes in capitalism.

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Alex J. Valentine is at the South African Herbal Science and Medicine Institute at the University of the Western Cape in Belleville, South Africa.

E-mail: alexvalentine@mac.com

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Drp1 phosphorylation and mitochondrial regulation

A paper by Cribbs & Strack (2007) in a recent issue of *EMBO Reports*, as well as an earlier study published by our group (Chang & Blackstone, 2007),

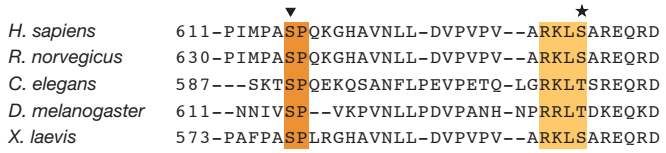

Fig 1 | Sequence alignment of the Drp1 sequence surrounding the PKA phosphorylation site in the indicated species. The position of the PKA phosphorylation site in Drp1 identified by Chang & Blackstone (2007) and Cribbs & Strack (2007) is indicated by an asterisk, and the consensus sequence is shaded in yellow. The position of the Cdk1/cyclin B phosphorylation site (Taguchi *et al*, 2007) is indicated by an arrowhead, and the consensus sequence is shown in orange. Both the PKA and Cdk1/cyclin B phosphorylation sites are conserved in all species shown. Boundary amino-acid residues are indicated to the left. Numbering for the rat sequence is derived from Cribbs & Strack (2007). Cdk1, cyclin-dependent kinase 1; Drp1, dynamin-related protein 1; PKA, cAMP-dependent protein kinase.

emphasize the important roles of protein phosphorylation by cAMP-dependent protein kinase (PKA) in the regulation of the dynamin-related protein 1 (Drp1) GTPase and mitochondrial fission. However, the Literature Report (Jahani-Asl & Slack, 2007) that accompanied the Cribbs & Strack article led to incorrect interpretations, which we would like to clarify here.

Foremost among these, the Literature Report discusses cAMP-dependent phosphorylation at Ser 637 in human Drp1 splice variant 1 (Chang & Blackstone, 2007) and Ser 656 in rat Drp1 splice variant 1 (Cribbs & Strack, 2007) as if they are distinct sites. However, both our study and that of Cribbs & Strack present sequence alignments that clearly indicate that these sites are the same; thus there is only one PKA phosphorylation site in Drp1 (Fig 1). In this regard, it is important to emphasize that there are several splice variants in the Drp1 protein and that protein size varies among species, making protein sequence alignments important when comparing results of studies investigating different species or variants. In addition, the Literature Report states that the Cribbs & Strack study showed that phosphorylation at this site attenuates GTPase activity. In fact, these authors reported no effect using a phosphomimetic substitution (Supplementary Figure 1C in Cribbs & Strack, 2007), although our study did report attenuation of GTPase activity in response to both direct phosphorylation by cAMP-dependent protein kinase, as well as with the same phosphomimetic mutant (Figure 3 in Chang & Blackstone, 2007). The reason for this discrepancy, despite using similar *in vitro* approaches and the same phosphomimetic mutation, is unclear; however, the attenuation of Drp1 GTPase activity that we observed would provide a mechanistic explanation for the findings in both papers that mitochondrial fission is impaired in cells, as well as for the resistance to pro-apoptotic stimuli reported by Cribbs & Strack.

Our study also showed that the intramolecular association of Drp1 is altered by the phosphomimetic substitution (Figure 2 in Chang & Blackstone, 2007); other mutations in the GTPase effector domain that alter intramolecular interactions also attenuate GTPase activity (Zhu *et al*, 2004). Even so, we cannot eliminate the possibility that conformational changes owing to phosphorylation at this site also affect interactions with other proteins involved in mitochondrial fission. Importantly, the two-dimensional phosphopeptide mapping experiments in our study showed that there is no basal phosphorylation at the PKA phosphorylation site in HeLa cells (Figure 1 in Chang & Blackstone, 2007), indicating that any regulation of Drp1 function by dephosphorylation at this site in these widely studied cells would need to occur in conjunction with activation of cAMP-PKA signalling. Conversely, we visualized other basal sites of Drp1 phosphorylation, one of which might correspond to a site of mitotic phosphorylation previously identified by Taguchi *et al* (2007).

The functional regulation of Drp1 by post-translational modifications such as protein phosphorylation, ubiquitination and sumoylation clearly provide cells with an impressive array of regulatory mechanisms to modulate mitochondrial morphology within cells. Further studies promise to clarify the role of these mechanisms in the dynamic regulation of mitochondrial morphology and distribution within cells.

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Chuang-Rung Chang & Craig Blackstone are at the Cellular Neurology Unit, National Institute of Neurological Disorders and Stroke, National Institutes of Health, Bethesda, Maryland 20892, USA
E-mail: blackstc@ninds.nih.gov
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Response by Arezu Jahani-Asl & Ruth S. Slack

A recent study by Cribbs & Strack (2007) identified a new mechanism for the integration of the second messengers Ca^{2+} and cAMP in the regulation of mitochondria form and function. This study was the first to provide a mechanistic link between phosphorylation of dynamin-related protein 1 (Drp1)—a component of mitochondrial fission machinery—and the regulation of apoptosis. Our report also referred extensively to two previous studies that investigated the role of DRP1 phosphorylation in mitochondrial fission: one study published by Chang & Blackstone (2007a) also identified a cAMP-dependent protein kinase (PKA) phosphorylation site on human DRP1, and a report by Taguchi *et al* (2007) showed that DRP1 is phosphorylated by Cdk1/cyclin B (Cdk1 for cyclin-dependent kinase 1) in a cell-cycle-dependent manner.