consistent with earlier observations seen after overexpression of rab4 (ref. 16). This effect required that rabenosyn-5 interact with rab4, as a rabenosyn-5 mutant lacking a rab4-binding site, or co-expression of a dominant-negative rab4 mutant and rabenosyn-5 did not elicit this phenotype. Because the transport assays were done *in vivo*, two scenarios could explain the effects seen after overexpression of rabenosyn-5. Either reduced transport to recycling endosomes is a consequence of enhanced rapid recycling, which would reduce the pool of transferrin available for the slow-recycling pathway. Alternatively, the primary effect of overexpressed rabenosyn-5 is a less efficient 'slow' recycling pathway, that might lead to compensatory upregulation of the 'fast' recycling route.

The interesting findings reported in this paper, as often, raise many additional questions. For instance, we would like to know whether effector-linking of rab protein domains can be extrapolated to the degradative branch of the endocytic pathway, or even heterotypic transport routes such as between endosomes and the Golgi complex. Intriguingly, rabaptin-5 also binds to rab33b, which is involved in retrograde transport through the Golgi complex[17]. On a different level, why are there at least three ubiquitously expressed bivalent effectors of rab5 and rab4. Perhaps rabenosyn-5, rabaptin-5 and rabaptin-5β act cooperatively to ensure a sufficiently strong physical link between the rab4 and rab5 domains. Alternatively, redundancy might be required because bifunctional rab effectors may act in parallel transport steps running from a given domain. Rabenosyn-5 is also known to be involved in delivering of newly synthesized cathepsin D from the Golgi complex to lysosomes[12]. It will be interesting to learn from further studies about this other function of rabenosyn-5. The exciting findings of de Renzis *et al.*[1] are of considerable interest, as they provide an appealing and testable model for the spatio-temporal coupling of entry to and exit from early endosomes, an endocytic sorting station that determines the fate of many biologically important proteins. □

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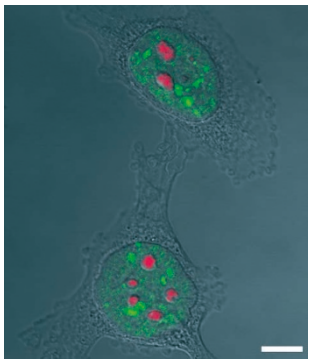
Proteomics of the nucleolus

Despite our increased understanding of the dynamic nature of the nucleus, and the heterogeneity of the suborganelles it contains, our knowledge of the factors they contain and the functions they mediate is still far from clear. One of the best-characterized suborganelles is the nucleolus, a nuclear body that mediates ribosome subunit biogenesis, and more recently has been implicated in other roles, such as transport of RNA. To determine if we have overlooked other equally critical components and functions of the nucleolus, the laboratories of Lamond and Mann have taken on the Herculian task of elucidating the proteome of this still-mysterious body (*Curr. Biol.* **12,** 1–11, 2002).

From purified nucleoli, Andersen and colleagues identified 271 proteins, of which over 30% were previously unidentified or uncharacterized. Identification of the isolated proteins were facilitated by directed searches of the draft human genome sequence. The nucleolar proteome that emerges is more complex than previously thought and supports additional roles for this suborganelle. For example, translation factors such as EIF5A, EIF4A1 and ETF1, which had not previously been shown to pre-assemble in the nucleolus, showed up in searches. This may support a role for nucleolar translation activity. To confirm that these were indeed *bona fide* nucleolar components, the authors constructed YFP fusion proteins with 18 of these factors. Of the 18 examined, 15 localized to nucleoli, in a variety of localization patterns. Next, Andersen and colleagues repeated the screen on cells in which transcription had been inhibited. They found that a subset of factors became enriched in nucleoli, suggesting that the nucleolus is a highly dynamic suborganelle whose molecular composition adapts to the metabolic state of the cell.

In addition, this work has also identified a new suborganelle – paraspeckles. In an accompanying paper from the same lab (*Curr. Biol.* **12,** 13–25, 2002), Fox and colleagues characterize one of the



novel factors, PSP1 (paraspeckle 1). PSP1 is recruited to the nucleolus after inhibition of transcription, but is localized to paraspeckles at steady state (the figure shows YFP–PSP1 in green and nucleolin, which localizes to the nucleolus, in red; scale bar 5 μm). Paraspeckles are found in the interchromatin space, generally at 10–20 copies per cell. Two other factors identified in the screen, PSP2 and p54/nrb are also localized here. So what is the function of this new body? The authors have observed that paraspeckles often colocalize with splicing speckles. Furthermore, when transcription is inhibited, paraspeckle factors relocalize to the nucleolar periphery. This suggests that, in common with the nucleolus, paraspeckles are dynamic bodies that respond to the changing environment of the cell. From the results so far, the authors speculate that paraspeckles may have a role in transcriptional regulation, although more work will be required to show that this is indeed the true function of this new body.

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