

Deciphering the nucleolar proteome

Yohann Couté[‡], Alexander Scherl[§], Catherine Déon[§], Aleth Callé[‡], Christine Hoogland[§],
Karine Kindbeiter[‡], Jean-Charles Sanchez[§], Anna Greco[‡], Denis Hochstrasser[§] and
Jean-Jacques Diaz[‡]

[§] Geneva Proteomics Centre, Central Clinical Chemistry Laboratory, Geneva University
Hospital, Rue Micheli-du-Crest 24, 1211 Genève 14, Switzerland.

[‡] INSERM U369, Faculté de Médecine Lyon-R.T.H. Laennec, Rue Guillaume Paradin,
69372 Lyon Cedex 08, France
diaz@laennec.univ-lyon1.fr

Nucleoli are nuclear domains that are known to be the site of ribosome synthesis for many years. Surprisingly, several recent data suggest that these sub-nuclear structures play also a crucial role in several other key events in the cell life. However, the molecular mechanisms governing the multiple functions of nucleoli remain to be determined.

To gain insight into the functions fulfilled by nucleoli, we have developed a proteomic analysis of highly purified nucleoli in order to determine their protein content. Nucleolar proteins have been separated by mono- and two-dimensional electrophoreses and identified by MALDI-TOF and nanoLC-ESI-Q-q-TOF mass spectrometry. 1-D and 2-D annotated maps of nucleolar proteins have been built (<http://www.expasy.org/cgi-bin/map1>).

This approach allowed to identify 213 different proteins. Remarkably, only 109 (51.2 %) of these proteins exhibited at least one known biological function, whereas the 104 (48.8 %) remaining ones did not display a well-defined biological function. Bioinformatic analyses allowed us to propose an hypothetical function for 43 of these 104 proteins. For example, a role in ribosome biogenesis was proposed for 31 out of the 43 proteins. However, despite extensive bioinformatic analyses, no function could be attributed for the 61 remaining proteins. Three of these latter have been expressed in human cells as EGFP fusion proteins and their intracellular localisation determined using confocal microscopy. Finally, the functional data available for the 109 proteins out of the 213 together with the assignment of hypothetical functions for 43 proteins permitted to group them into different functional classes reinforcing the notion of a "plurifunctional nucleolus". Notably, the finding that several proteins involved in several steps of mRNA metabolism suggested that nucleoli may play an important role in the post-transcriptional control of gene expression.