during the acute phase of a traumatic brain injury a ty of growth factors, cytokines and inflammatory iators are released. Here we investigated the temporal ct of cerebral tissue extract from traumatically-injured on the differentiation of cultured embryonic stem cells. **hods:** Sprague-Dawley rats were subjected to lateral percussion traumatic brain injury (TBI). Brain extracts derived by pooling and homogenising the respective ispheres of three traumatised or healthy rats. Mouse yonic stem cells (CGR8) were grown under standard ure conditions for two days on gelatine-coated 6 well s. Subsequently, FCS was omitted (control, CTRL) extract from traumatised (trauma extract, TE) or hy rats (healthy extract, HE) was added at a centration of 20%. Cells grown under standard culture itions were used as standard (STD). All experimental obtained are presented as percentage of standard es. After 3, 5 and 7 days total RNA was isolated and differentiation status of the co-cultured stem cells was ssed by amplifying stem cell specific marker OCT4, enitor cell marker nestin and neuronal marker MAP2 g real-time PCR. **Results:** We observed a significant ease of OCT4 expression after 5 (0,85 ± 0,011; p<0,05) 7 days (0,87 ± 0,013; p<0,01) in TE treated cells as pared to standard values, indicating an onset of erentiation. Reduced Oct4 expression observed at any point in control or HE treated cells was not statistically ificant. An increase of nestin expression could be rved in all groups after only 3 days, though a ificant increase was only demonstrated in TE treated (1,92 ± 0,059; p<0,01). Nestin expression in HE ed cells peaked on day 5 (1,68 ± 0,036; p<0,05). On 7, nestin expression declined in all groups. In TE ed cells expression of neuronal marker MAP2 was ginally increased at day 3 and remained constant at later points. However, values remained below the values of taneous differentiation in control cells. In HE treated MAP2 expression was elevated as compared to taneous differentiation in control cells after 5 days of bation. However, values obtained at this time point not significant. **Conclusion:** A decrease in Oct4 ession and increase in nestin expression is associated the onset of differentiation of stem cells into enitor cells. TE dependent reduction of OCT4 ession and rapid TE dependent upregulation of nestin ession indicates that trauma extract strongly induces cell differentiation. This is in accordance with the ificant decrease of nestin after 7 days of TE treatment, nestin is only transiently expressed during early rentiation of stem cells. However, our results also gest that TE does not seem to induce neuronal rentiation, since MAP2 expression was hardly altered during long term TE stimulation of stem cells. MAP2 ession was elevated during incubation of stem cells extract from healthy rats, indicating healthy brain to ort neuronal differentiation pathways. These results rate a strong micro-environmental affect on stem cell differentiation pathways. Such observations should be taken into account when considering therapeutic cell replacement strategies. Presently, the impact of injured environment on stem cell differentiation pathways is being examined in more detail.

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PULMONARY OXIDATIVE STRESS, INFLAMMATION, AND FIBROSIS INDUCED BY CARBON NANOTUBES. E. Kisin[1], A.R. Murray[3], V. Johnson[2], O. Gorelik[4,5], S. Arepalli[4,5], V.Z. Gandelsman[4,5], A.F. Hubbs[1], R.R. Mercer[1,3], P. Baron[6], V.E. Kagan[7], A.I. Potapovich[7], V. Castranova[1,3,7] and A.A. Shvedova[1,3].

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Society is currently amidst a revolutionary development of remarkable new technologies based on novel applications of nanomaterials. From drug delivery tools and micro-circuitry elements to microcomputer networks and super-durable composite materials – this is just an illustration of the unprecendentedly broad range of applications and approaches using nanomaterials. One of the most interesting examples of nanoimaterials are carbon nanotubes (CNT), new members of carbon allotropes similar to fullerenes and graphite. Previously, we reported that exposure of human bronchial epithelial cells to CNT induced oxidative stress, depletion of antioxidants, morphological changes, cytotoxicity, and apoptosis. In the current study, we investigated pulmonary toxicity of CNT after pharyngeal aspiration by C57BL/6 mice. We found that CNT caused dose-dependent formation of granulomatous bronchointerstitial pneumonia, fibrosis (collagen accumulation), and changed pulmonary function. Administration of carbon nanotubes to C57BL/6 mice also resulted in a dose-dependent augmentation of biomarkers of inflammation quantified by bronchoalveolar lavage (BAL) cell counts, total protein, lactate dehydrogenase (LDH) and g-glutamyltranspeptidase (GGT) activities in BAL fluids and accumulation of pro-inflammatory and pro-fibrotic cytokines. CNT induced release of pro-inflammatory and pro-fibrotic cytokines from macrophages in vitro. Overall, our data suggest that exposure to CNT leads to pulmonary toxicity realized through synergized interactions of inflammatory response and oxidative stress culminating in the development of multifocal granulomatous pneumonia and fibrosis.