The aim of the project is to identify the elusive Small Copper Carrier (SCC), indicated previously by to be a relatively small molecule, which is supposed to bind the Cu^{2+} ions and participate in their transport in the blood of many, perhaps all mammals. SCC was partially isolated initially from the blood of experimental animals providing features of Wilson's disease, a genetic disorder resulting in accumulation of copper in liver, other organs and also blood. Such uncontrolled copper deposits have a broad spectrum of toxicity, including mental retardation. SCC was also found, at much lower amounts, in the blood of healthy humans, and also sheep, cows, pigs and mice. However, it has not been purified and was characterized only partially, which is quite surprising. The reported difficulties in identifying its chemical nature are rather mysterious. It has been speculated that SCC comprises the so-called labile blood copper. This is a pool of copper ions determined after removal of blood proteins that bind copper, mostly ceruloplasmin and albumin. The labile blood copper was increased in many cases of Alzheimer's disease (AD). It was also noted in type 2 diabetes, and a number of cancers. Copper is an essential microelement in Eukaryotes, because it is required for oxygen utilization, via the cytochrome c oxidase in mitochondria and detoxication via Cu/Zn superoxide dismutase in cytosol. Therefore each cell of the human body must be adequately supplemented with copper ions delivered by blood. Copper is collected from food in the small intestine and then transported to liver, where two major copper proteins in blood, ceruloplasmin and albumin (HSA in humans) are biosynthesized, with a small remainder of copper, perhaps 2% or less of the total, bound to low molecular weight ligands, presumably SCC. Two general views focus on HSA and SCC as candidates to play this role. Elucidating the composition, structure, stability and kinetic properties of SCC will be therefore instrumental in identifying it as a beneficial or toxic species in AD and other diseases. Copper is also a cofactor of many novel anticancer drugs. It is necessary to understand how it is carried around in the bloodstream to find out whether it should be a target of pharmacological intervention and what properties should putative copper or anticopper drugs have to be effective. Fetal Calf Serum (FCS) is the cell-free fraction of bovine fetal blood, comprising more than 1000 components, many of which have not been characterized. FCS is necessary to support the growth of cultured eukaryotic cells, which must necessarily include the copper delivery. We therefore hypothesized that FCS should contain SCC. FCS is a certified laboratory reagent available in large amounts, making it a perfect choice for the large scale SCC isolation. A conceptual problem with SCC is that the high concentration and high Cu(II) affinity of HSA pose a stringent limit on the properties of SCC to be able to compete for Cu^{2+} ions. This requires that SCC has the Cu(II) affinity higher than expected from its spectroscopic properties or is more highly concentrated in blood than HSA, hence millimolar. The following resulting options should be considered here: **(i)** SCC complex has unusual structure with high affinity; **(ii)** SCC is ternary complex or family of such complexes; **(iii)** SCC is kinetically rather than thermodynamically stable; **(iv)** SCC is an artifact. We propose the following research plan to clarify these points, which is divided into four tasks. In Task 1. SCC and other Cu(II) carriers in FCS will be identified by fractionation, with respect to their copper binding and molecular mass, helping solve problem (iv). In Task 2. the identified SCC candidate(s) will be synthesized in large quantities and their Cu(II) complexes characterized by in terms of structure, Cu(II) affinity and susceptibility to Cu(II) reduction to Cu(I). Task 2 results will respond to problems (i) and (ii). In Task 3. the time dimension of SCC activity will be studied with respect to copper exchange properties, in comparison with HSA. The issue of reaction rates is critical for the whole project, because it can validate whether SCC is a functional partner of copper distribution system, hence a player in human health and disease. The research will include studies of Cu^{2+} and Cu^{+} reactions with HSA, SCC from Task 2 and other small molecules present in blood, which may act as catalysts or inhibitors of the binding/exchange reactions. Our instrument is limited to reaction times longer than 2 ms. Studies at shorter times will be performed during the 6 months research stay of the doctoral student in TU Delft. The completed Task 3 will provide response to problem (iii). The ultimate test of function of SCC will be made in Task 4. in which the ability of SCC to deliver copper to cultured HEK293 cells will be tested using a methodology developed in our laboratory. As control experiments, also the FCS and whole FCS fractions will be tested. These studies will help complete the SCC story, empowering us to formulate physiological hypotheses and plan biological experiments. The project is not without risks. SCC might be an artifact or a pathological species. Its function may be conveyed by known carriers, e.g. HSA or histidine. The project design is resistant to these threats, because rather than following the literature on SCC, it includes its comprehensive verification. Alternatively, SCC may exist, but not in FCS. If such unlikely conclusion is obtained in the project, it will nevertheless provide a broad body of data on copper handling in blood, to be used in future studies. All methodology planned to be used is robust and tested, ensuring the project execution. All required instruments are fully available, directly at IBB or by the established collaborations.